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ARTICLE I.

The Annual Discourse.

SOME ABUSES IN SURGICAL PRACTICE.

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SOME ABUSES IN SURGICAL PRACTICE.

THE custom of having a formal oration at the annual meeting of the Massachusetts Medical Society was instituted in 1804, and on only six occasions since then, has its orator failed to deliver his message of hope and reminiscence.

The list of subjects embraces almost all the questions which have perplexed and agitated the medical world during these 100 years, and in the list oforato rs are to be found the names of those who upheld and advanced the professional standards of this Society during the 19th century, — the Warrens, Bigelows, Jacksons, Shattucks, Holmes, Homans, and many other equally eminent exponents of medical education and practice. For the privilege of being enrolled in such distinguished company, I am deeply grateful, and desire to express my appreciation of the honor you have conferred upon me.

In the earlier orations, it was customary to refer at the beginning to those Fellows who had fallen from the ranks during the year, whose memories were thus affectionately recalled, and whose services in the cause of humanity appropriately recorded. So long as the membership of the Society was small, and intimate mutual acquaintance and friendships existed, such a custom possessed a sincerity and a value, that the growth in numbers make obviously impossible.

I think, however, that we should do well even now, to pause occasionally in the midst of the increasingly absorbing activities of our daily life, to testify to our grateful appre-

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ciation of the memories of those of our Fellows who have
ceased to labor, but whose good works and faithful service
are a constant inspiration and stimulus for us who have the
burden still to carry.

I think you will pardon me, if I refer but for a moment,
to two particularly distinguished and beloved Fellows of
this Society who were with us a year ago, but whose faces
we miss today.   Seldom are we called upon to mourn two
such men as Maurice Howe Richardson and Arthur Tracy
Cabot, in a single year.   Two years ago, Dr. Richardson
delivered the annual oration before this Society, and for
more than thirty years he has been a frequent and valued
contributor to our society proceedings.

His inspiring presence, and the simple, sincere, and ab-
solutely frank manner in which he gave the results of his
observations and his extraordinary experience, gave to all
that he said, an authority and a charm, that made him a
most welcome guest at medical gatherings all over the
country.   It would be hard to say whether we loved him
most as teacher, hospital chief, operator, consultant or
friend; association with him in any capacity was a pleasure
and an inspiration, which those who were favored with it
can never forget.

Dr. Cabot, too, was long a faithful and effective worker
in behalf of this Society, and of the ideals for which it
stands, serving as its President during 1904 and 1905.   A
distinguished surgeon, a man of broad culture, interested in
art, letters and education, to all of which he rendered sub-
stantial service, he touched life on many sides, to the ad-
vantage and honor of them all.

In the midst of an active professional life, devoted chiefly
to surgery, he found time to give us an example of devotion
to great questions of public health and the prevention of
disease, which is worthy of the best traditions of the scholar
in medicine.

One feature of these two lives, as they touched each other, should not be overlooked. Starting in practice at the same time, and in the same community, attached to the same hospital, and devoted to the same line of practice, they continued through life, an intimate friendship and mutual confidence and esteem, which was never marred by any of the jealousies and quarrels that have so often impressed the history of medicine. They have given us an example of that kind of professional comradeship which we all admire, but so often fail to live up to, and have taught us that in medicine, at least among the really great, envy and jealousy have no place.

Among the earlier orations delivered before this Society, there was one that has always been of especial interest to me, which I have read and re-read many times, and which is, I think, worthy a place among the classics of our medical literature. The orator was Dr. Jacob Bigelow[1], and the subject was "Self Limited Diseases." It was delivered at the annual meeting in 1835, and was a calm, logical, and very powerful arraignment of the prevailing practice of over-medication, and of the unreasonable faith which the profession of that day seemed to have, in the efficacy of drugs as a means of altering the natural course of many of the diseases that then were, and still are, common in New England.

He defined a self-limited disease as "one which receives limits from its own nature, and not from foreign influences; one which, after it has obtained a foothold in the system, cannot, in the present state of our knowledge, be eradicated or abridged by art; but to which there is due a certain succession of processes to be completed in a certain time — which time and processes may vary with the constitution and condition of the patient, and may tend to death or recovery, and are not known to be shortened or greatly changed by medical treatment."

Then he proceeded to show that these self-limited diseases fell under three heads: — "the simple, in which the disease observes a continuous time, and mostly a definite seat, such as the eruptive fevers for example; the paroxysmal, in which the disease, having apparently disappeared, returns at its own periods, like epilepsy, angina pectoris and asthma; and the metastatic, in which the disease undergoes metastasis or spontaneous change of place, like mumps, gonorrhea and acute articular rheumatism."

The prevailing practice then was to treat all of these with the so-called shot gun prescriptions, which were popular in those days; to claim the cures to be the result of the treatment, and the deaths, to be the hand of God. "A charm," he says, "is popularly attached to what is called an active, bold, or heroic practice, and a corresponding reproach awaits the opposite course, which is cautious, palliative and expectant."

And he concludes his masterly argument against over-zealous interference by saying, "that the longer and the more philosophically we contemplate this subject, the more obvious it will appear, that the physician is but the minister and servant of nature; that in cases like those which have been engaging our consideration, we can do little more than follow in the train of disease, and endeavor to aid nature in her salutary intentions, and to remove obstacles from her path."

All this sounds very natural, almost commonplace to-day, but it was revolutionary then. The days of our confidence in the efficacy of drugs and of over-medication, are happily long since passed. But I have often felt in considerable doubt as to whether there were not other directions in which we, at the present time, have not failed to put enough confidence in the healing powers of nature, and were not still putting too much faith in the power of our own hands; that it was pertinent for us to inquire, even if

there is no over-medication in medicine, is there no over-interference in the practice of surgery?

In no department of our profession have we witnessed such wonderful and such beneficent progress, since the days of Jacob Bigelow, as in the department of surgery. The discovery of anesthesia, with the more recent introduction of new anesthetic agents, and new methods of administration, which have rendered anesthesia safer and more effective, banished pain, and made careful, deliberate and accurate dissection of the living body possible, — the discovery of asepsis, which robbed the period of convalescence of its greatest terrors, laid bare the secrets of visceral pathology in the living, and made the cavities of the body as accessible to surgery as the surface, — and animal experimentation, which by making it possible for us to test the effect of many surgical procedures before applying them to man, has been of incalculable benefit in helping us to develop a safe and efficient surgical technic, and has been the means of discovering the value of serum therapy, one of the most important discoveries ever made for the prevention of disease, as well as for its relief, — all of these, anesthesia, asepsis, and animal experimentation, have been the important determining factors in the extraordinary development and growth of modern surgery, the history of which has been a source of the greatest pride and satisfaction to every friend of our profession, as its progress has been of incalculable benefit to humanity. It is much pleasanter to record the triumphs of modern surgery, than to criticize its abuses; and the temptation to dwell upon its achievements, and especially the achievements of American surgery, is particularly strong.

But although we may very properly treat with contempt, such criticisms as are contained in Bernard Shaw's "Doctor's Dilemma," which reflects the depths of pessimism and is simply ill-natured, unfounded abuse, is it not worth while

occasionally to pause in so uninterrupted a triumphal march, to see that the camp followers and retainers, who always follow in the train of a victorious army, are kept in their proper places, and that the fruits of the victory are not lost through the excesses of the victors?

The glamor of surgery, its directness of attack, and its tangible results make it particularly attractive to all medical students, and inspire the majority of them with an ambition to practice it. Surgery, too, occupies by far the larger part of our hospital equipment, and has led to the establishment of numerous small community hospitals which are chiefly surgical; one of the most obvious results of which has been that the local practitioner feels obliged to undertake surgery, just as he feels obliged to undertake obstetrics, in order to protect and develop his general practice.

Sir Patrick Cullen's observation, "that chloroform has done a lot of harm, it has enabled every fool to become a surgeon," has become still less an exaggeration of the truth, since the discovery of asepsis.

Now, while the evolution of medical practice has been in the direction of greater simplicity, less dependence upon drugs, and less meddlesome interference with nature, the resort to surgery has appealed more strongly than ever to the progressive, reforming spirit of our generation, and active interference has been invoked for the relief of all sorts of disorders, both functional and organic, in many cases with but little justification, and it has been freely practised by men whose training and opportunities for the observation and interpretation of living pathology, have been far from adequate.

Until within a few years surgical interference was employed chiefly for the relief of the accidents and emergencies of life, and operations were but a small part of the surgeon's duty, strictly limited to cases of absolute necessity.

It is perhaps entirely natural, therefore, that with the removal of the restraints imposed by pain and septic inflammation, and the demonstration of the safety and practicability of operation, we should find ourselves carried to the opposite extreme, operating often when our interference is ill-timed and unnecessary.

Having demonstrated our ability to open and explore all the cavities of the body, to remove much that they contain, and to rearrange more, without imperilling life, it seems to me that our efforts should be directed now, with still greater energy, to determining the limits within which our interference is necessary and desirable.

In connection with such great gatherings as the Surgical Congress, held in New York last autumn, I think we should be particularly careful not to permit ourselves to be so carried away by the number and variety of operations, and the wonderful exhibition of surgical prowess, as to lose sight of what is after all, the only justification for surgical interference at all, viz., the relief of suffering, with as little danger, distress and mutilation as possible.

Then, too, we must never overlook the effect of such clinics on the ambitions of untrained men, — men who are dazzled by the brilliancy of the achievements, and are tempted to imitate them, but who have not had the training or experience to qualify them to discriminate between the time when such operations are useful and proper, from the time when they are unnecessary and improper.

The most significant and important results of that Congress, as it seems to me, were the recognition of the fact that major surgical operations are being advised and undertaken by men with little or no surgical experience, and the call for some action on the part of the profession to safeguard the science of surgery and the public from the practice of untrained and incompetent men.

The ability to do major surgical operations, and to get by

with them, to use a slang expression, because the wounds
heal perfectly, is, I think, a serious menace, not only to the
public, but to surgery itself; and we look forward with
great interest and hope, to the efforts of the new College of
Surgery, conceived in New York last October, and borne in
Washington last month, so to standardize the require-
ments for the practice of surgery as to discredit, and as far
as possible eliminate, the incompetent.

But it is not altogether to the abuses that are incident to
incompetency, important and glaring as these are, that I
wish particularly to direct your attention. In an article
on "Conservatism in Surgery," by Dr. James E. Moore,[2]
one of the most distinguished surgeons of the Northwest,
"surgeons are divided into three classes, the conservative,
the radical, and the progressive."

"The conservative is the man who treats empyema medi-
cally or with the aspirator, who temporizes with tumors of
the breast until their malignancy is established beyond a
doubt, and the chances for a thorough excision are lost;
who waits for the development of a tumor in acute inflam-
mation of the appendix; who waits in cases of intestinal
obstruction until operation is almost hopeless, and by a
general policy of delay and attempted palliation fails to
grasp the opportunity for safe and successful interference."

The type is now chiefly of historical interest, so completely
has it disappeared in the rise of the radical surgeon, who is
described by Dr. Moore as one "who frequently performs
unnecessary, and even unwarrantable operations," does
gastro-enterostomy, "when stenosis did not exist, or when
the operation could not rationally be expected to do any
good," anchors a floating kidney, "when, because of a
general ptosis of the abdominal organs, there is no possi-
bility of relief;" "removes the appendix for insufficient
reasons, because it is such a common offender that people
are very ready to accept a diagnosis of appendicitis on a

very small array of symptoms," and so on through the list.

This type is, it seems to me, unfortunately too common, and judging from my own observation, is still increasing. Moore very properly adds, "that some operations should be radical, but no surgeon should be so." The safe, sane, well-balanced surgeon, who holds his course between these two extremes, he calls the progressive, — a title that is well enough if you can forget the ordinary modern use of the term in politics and religion.

It is the increasing influence of the radical that prompted Dr. Richardson[3] to say, "that there is a tendency quite prevalent among surgeons to make light of surgical operations. I cannot but regard this as an evil, for all surgical operations, no matter how apparently trivial, are attended by possible difficulties and dangers which should always be taken justly into account in discussing their pros and cons."

This tendency to make light of operations is still further illustrated by the closing sentence of a most interesting and valuable paper by Bloodgood,[4] on "Medical Aspects of Surgical Diseases, or Preventative Surgery," in which he asks the question, "Why should not surgery interfere in the least dangerous period, even if it interferes now and then unnecessarily?"

A question which is, I think, sufficiently answered in an earlier sentence of the same address, in which he says, "Appendectomy in doubtful acute attacks, and in the free interval after such attacks, has been too often performed when the real trouble was gastric or duodenal ulcer, gall stones, renal colic, ptosis of the colon, pericolitis, or pelvic lesions, or in some cases, the abdominal symptoms of tuberculosis or pernicious anemia," and he might well have added, in some cases when there was no demonstrable lesion at all. When he concludes that "this over-zealousness in ap-

pendectomy has practically done little harm," I cannot
follow him.

Of course it has done, and can do, little harm in his hands
because he would make such mistakes only when the most
careful history taking and physical examination made them
unavoidable, but to preach such doctrine to the average
operating surgeon throughout the country, seems to me
hardly fair to those who put their health and their lives in
our hands.

If we look back over the history of modern surgery, we
shall find many procedures which we once believed to be
sound and beneficial, which have since been entirely aban-
doned or greatly limited and modified in later practice, and
more that are still in vogue, whose limitations we are just
beginning to appreciate.

When the danger of peritonitis was removed, and the
safety of opening the abdominal cavity demonstrated, one
of the first popular procedures was Battey's operation, or
the removal of the normal ovaries for the relief of pelvic
pain, and although this has long since been given up, every
hospital pathologist can testify to the number of practically
normal uterine appendages that are sent to his laboratory,
as examples of chronic ovaritis, and every surgeon has felt
the disappointment that has followed when their removal
has failed to give the hoped-for relief, and the family physi-
cian has found himself after the operation up against the
same old problems.

Then our attention was diverted to the Fallopian tubes,
and the presence of a few adhesions and a little dilation has
led to their removal with as little satisfaction to patient
and physician. Please remember that I am not speaking
of those cases in which marked anatomical changes are
found, and where unspeakable relief has followed the re-
moval of seriously diseased appendages, but of those in
which no gross lesions could be detected upon examination,

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yet operation was undertaken, because there seemed to be
nothing else to do, and no adequate cause was disclosed by
the pathologist's report.

Then think how few years it is since the repair of the
cervix uteri was regarded as a most important step in the
cure of a great variety of disorders of supposed reflex origin,
without much regard to the extent of the tear or to the
presence of eversion or erosion.   It was an almost unlimited
field, and for years it was thoroughly exploited, but we
have learned now that it has very definite and obvious
limitations within which it is still a most useful and neces-
sary procedure.   Much the same can be said about the
operation for the correction of backward displacements of
the uterus.

Its value in cases where definite symptoms exist directly
traceable to the displacement is, and probably always will
be unquestioned, but that it should be undertaken when-
ever, in the course of a thorough physical examination the
uterus is found retroverted or retroflexed, seems absurd, not
because any of the procedures for correcting the displace-
ment are dangerous, but because in default of positive in-
dications, confirmed if possible, and it generally is possible
by a preliminary mechanical replacement, they seem to be
a needless meddlesome sort of interference.

Yet because it is safe, simple, and gratifies the passion for
doing something, or having something done, it is frequently
employed when the symptoms and the displacement can
have no possible relation.

Leaving the pelvis, we come to the question of appen-
dicitis, — perhaps the most popular operation of modern
times, with the laity as well as with the profession.   In the
first place, let me state as emphatically as possible, that I
stand squarely with those who believe that in acute ap-
pendicitis operation should be done as soon as the diagnosis
is clear — preferably within the first 24 or 48 hours; that

with a history of one or more well defined attacks, the re-
moval of the appendix is desirable on account of the proba-
bility of recurrence, and that in many cases of chronic
abdominal distress, if there is local pain or tenderness, with
or without muscular spasm, its removal is justifiable on
suspicion.

But although trying to be as careful as possible in diag-
nosis, I have many times operated when the subsequent
history, or the condition of the removed appendix demon-
strated the error of having operated at all; sometimes when
I have yielded to the importunities of the family physician,
or of the patient himself, and sometimes when my own
judgment was at fault; and I think that if the pathologist
of any of our large hospitals would compile the results of
the examinations of the appendices sent to his laboratory
during a year he would be the only one not surprised at the
large percentage of practically normal specimens.

In how great a number of the cases of chronic abdominal
distress which present themselves at our large surgical
clinics, do we find that the appendix has already been re-
moved, but without relief; and how often do we find that
adhesions, hernia or infection have made the patient even
worse off than before?

My own feeling is that we need to exercise far greater
care than we do, in making the differential diagnosis in
cases of appendicitis, — that no one should operate for a
simple appendicitis, who is not sufficiently trained by ex-
perience, and by his observation of living pathology, to be
able to detect the rarer and more complicated conditions,
for which appendicitis may be mistaken. Hasty snap-shot
diagnosis have certainly led to much ill-advised and un-
necessary operating.

In the surgery of the gall bladder, operations are still far
too common, in which the expected gall stones cannot be
found or an ulcer of the duodenum is overlooked, and in

which the drainage of the gall bladder is, therefore, quite
superfluous.

The complexity of the anatomical relations in this region
make accurate diagnosis, even after exposure of the field,
much more difficult than in the region of the appendix; but
this is of small comfort to the victim of an unnecessary opera-
tion, or of an unrecognized but troublesome duodenal ulcer.

In considering these surgical abuses and the limitations
they ought to impose on surgical practice, the history of the
operation of gastro-enterostomy is, I think, particularly
significant.   As a means of curing all sorts of intractable
dyspepsias, as was for a time confidently expected, and as it
is still far too commonly practiced, it has proved to be most
disappointing; but as a means of relieving pyloric obstruc-
tion, or as an adjunct to pyloric resection, its results are ex-
ceedingly gratifying.   Its limitations are, however, not even
yet as generally recognized and accepted as they ought to
be, and when disregarded, they lead to some of the most
deplorable illustrations of unnecessary and misdirected
surgical interference.

Movable kidney has been another easy mark for the
over-zealous surgeon.   It may give rise to severe and seri-
ous local discomfort, as in the occurrence of Dietl's crises,
and its fixation in correct position may then be accomplished
with great relief, but it is far more commonly a part of a
general visceral ptosis, the discomfort from which is not at
all removed by a simple nephopexy.

All of these are useful and necessary operations, but they
illustrate, it seems to me, certain abuses which have grad-
ually, and perhaps naturally, crept into the practice of
surgery, abuses which are not the result of incompetency,
but are due sometimes to a faulty interpretation of a case
history, more often to over-confidence in the benefits to be
derived from mechanical interference, and an unrestrained
enthusiasm for doing something tangible and heroic.

It is not a sufficient answer to say that these operations are devoid of danger, and of post-operative complications — they are reasonably so, it is true, in the hands of trained experts, but they are not absolutely so, by any means, in the hands of the average operator throughout the country, and even when performed by experts there are "Certain Unavoidable Calamities Following Surgical Operations," as was pointed out by Dr. Richardson [5] in a paper before the American Surgical Association in 1904, such as hemorrhage, thrombosis, embolism, and suppression of urine. I have never had a death from suppression of urine, except when its possibility was anticipated, but I have had unexpectedly fatal results from hemorrhage and embolism.

If I should permit my son to be operated on for a mere suspicion of some chronic inflammatory trouble about the appendix, and one of these accidents should occur, I hope I should have the grace to forgive, but I never should be able to forget, the tragedy of his death, and if the event of the operation should prove my mere suspicions unfounded, I am sure that I should never forgive myself for the sacrifice of his life.

I do not conceive that a surgeon's duty to his own son is any different from his duty to somebody else's son. I realize fully the responsibility which he is obliged to accept whenever he recommends operation, and I would not by any means have him shirk it; but I do insist that he should not undertake such operations, as I have been discussing, lightly or without having carefully balanced the patient's present disability and suffering, its probable course if not operated on, and the accuracy of his diagnosis, against the dangers which are inherent in every surgical procedure.

But it is not at all necessary to have a fatal result to be brought in contact with the limitation and abuse of surgery. Consider for a moment the cases, and they are numerous enough in the experience of every one of us, I know they

are in mine, and I do not believe my experience in this re-
spect differs much from that of others similarly situated,
the cases in which, after operation, the relief is not perma-
nent, is not even transient, — where the only result is the
substitution of one form of complaint or disability for an-
other, that large class of cases in which we find no very
definite physical signs, no clearly defined pathology, but
many and distressing subjective symptoms. And after the
failure to relieve by operation, we explain it by saying that
the patient is a neurotic or a neurasthenic and that she be-
longs in the category of those who were so well described
by Cheever, "as satisfied only when their pocketbook and
their pelvis were both empty." But the point which I
want to make is, shouldn't we have known that the patient
belonged to that class, and if belonging to that class explains
and excuses the failure of the operation, are there not some
very obvious limitations to be applied to the practice of
surgery in that class of patients, and ought they not to be
recognized and applied before, not after, the operation?

Now let us look for a moment at the surgery of malignant
disease, which presents a different problem. It must al-
ways be an open question, how far operations are worth
while, which involve a serious deformity, like extirpation of
the tongue and larynx, or resection of the esophagus, or
permanent colostomy.

If we could reasonably expect as a result of these pro-
cedures, a considerable prolongation of enjoyable life, or
less suffering from the recurrence than from the original
disease, there could be no question of their desirability or of
our duty to urge their performance.

But in my own experience and observation such un-
fortunates usually eke out a short and very uncomfortable
career, and the progress of the recurrent disease is quite as
distressing as that of the original. Much the same can be
said of the late operations for malignant disease wherever

situated. It is perfectly true, that thorough extirpation offers the only means of relief in malignant disease, but it is equally true, that to be effective at all, it must be applied early.

Bloodgood[5] has pointed out with especial force, the possibility of recognizing the precancerous stage of malignant disease in the stomach and elsewhere, and the false conservatism that permits a recognized ulcer or tumor to pass from the benign into the malignant stage, cannot be too strongly condemned. At the same time, I believe that we should be brave enough to refrain from the mutilation and suffering caused by too late and hopeless operations.

Graves' disease is another illustration of the excesses into which our surgical enthusiasms are apt to lead us. We should all agree, that in the early stages, many of these cases recover a reasonable degree of health under appropriate medical and hygienic treatment, and that in the late stages of the disease, operative treatment is often unsatisfactory and even dangerous.

But that early operation would result in greater assurance of permanent benefit to a greater number than if it were confined to those who failed to respond to a reasonable trial of palliative treatment, is by no means proven. Of course it would be safer, and the period of convalescence much shorter, than when the operation is delayed too long, but is it necessary — is it indicated?

Knowing that so many cases when taken early, yield to less severe measures, it seems to me that such measures should have a reasonable trial, ever keeping in mind that failure to respond promptly should lead to their abandonment in favor of operation without any unnecessary delay.

I will simply mention the exploratory incision for diagnostic purposes, because the possibility of its abuse is too obvious, and illustrations too common to require further comment.

Now although all of the operations which I have referred to have their proper place, and are often imperatively demanded, the diseases for the relief of which they are undertaken are by no means always fatal or even permanently disabling under less heroic treatment. Just how large a proportion would recover under medical care has never been accurately determined, and until we have some definite statistics bearing on this point, our discussion must be based very largely upon the unsatisfactory and unscientific data supplied by personal experience and impressions.

It is equally difficult to get at the proportion of operative failures, failures not because of mortality, but because the symptoms for which the operation was undertaken, were not relieved.

Some quite significant figures were quoted in a paper which was read by Dr. Dwight, before this Society two years ago, on "The Prevalence of Circulatory Diseases in New England," and they are of special value, because compiled without any reference to the subject which we are discussing.

They were taken from the census reports, and show the changes that had taken place between 1900 and 1908, in the relative frequency of the more common diseases, tabulated as causes of death per 100,000 of the population.

They showed that in the preventable and infectious diseases, except scarlet fever, there was a very marked diminution, as illustrated by this death-rate; that in the circulatory diseases, except pericarditis, there was an almost equally marked increase.

In the group of "All Other Diseases" there was, of course, no such uniformity, but the significance lies in the fact that appendicitis, biliary calculi, ulcer of the stomach, intestinal obstruction and hernia, diseases in which surgical interference has been particularly active, all present a slightly increased mortality per 100,000 of the population. The in-

crease in the number of operations during this period must have been very large; and yet the statistical results fail to indicate the degree of improvement which the more radical operators would have us believe, should follow more radical and more frequent interference.

Although all of the illustrations thus far referred to have been taken from the domain of general surgery, the different specialties are by no means exempt from the same tendency to operative excesses. Witness the muscle cutting operations of the oculists, the removal of tonsils and adenoids by the laryngologist, of nasal spurs by the rhinologist, and the extraordinary increase in the number of mastoid operations by the otologist, — all of these, like the others, are eminently useful and necessary procedures; but the indications for their performance are easily exaggerated by the enthusiasm and zeal of an impatient attendant.

I shall not weary you with any further illustrations, but shall be quite content if I have been able to convey to you the lesson which Jacob Bigelow's talk on "Self Limited Diseases" suggests to me, viz., that we should be careful not to put too much confidence in the work of our own hands. In thus recalling the faith of the fathers in Nature, I must disclaim again any desire to pose as a reactionist, or even as an ultra conservative. It is the glory of surgery that it is able to

> Rally the scattered
> Causes and that line
> Which nature twists,
> Be able to untwine.

And no one can measure the benefit of humanity of the growth and expansion of surgical practice. Nor would anyone for a moment wish to do anything but encourage and applaud the pioneer work in surgery, which is being carried on in our great laboratories and hospitals.

But as applied to the every day practice of the average operator, it must be acknowledged, that surgical interference should be undertaken, only after a most careful and thorough study of the conditions for which relief is sought, of the methods which may be employed to secure it; and by men whose training and experience qualify them to meet intelligently the dangers and complications that may be encountered.

We should not fail to recognize the fact that all of these surgical operations are definitely limited in usefulness and applicability, and that disregard of these natural limitations, constitutes a serious abuse of what is a perfectly legitimate means of relief when properly indicated.

It seems to me that the purely mechanical side of surgery has been receiving far too large a share of our attention, for we are not merely mechanics or carpenters. We must not forget that "any operation which does not better the condition of the patient must be regarded as a therapeutic error,"[8] and that to possess a sound judgment as to the indications and counter-indications for operations, based upon a careful and thorough knowledge of the natural history of disease and of surgical pathology, is far more important and valuable than the acquirement of mere mechanical skill.

In no department of human life are new methods more eagerly grasped at and tried out than in medicine and surgery; and the discovery that the cavities of the human body can be safely explored, and their contents removed or re-arranged, has very much overshadowed our interest in surgery as a science, and very much over-stimulated our enthusiasm for its practice as an art.

But all this will be changed. The only question is how, and by whom, the change shall be brought about. Shall it be slowly and gradually, by the natural processes of evolution; shall it be forced upon us by a popular demand for

the safeguarding of surgical practice; or shall it be accomplished by the efforts of the profession itself, to secure a more thorough preliminary training, and adequate hospital apprenticeship for all students who are intending to engage in the practice of surgery?

I believe that it can be done best, and that it will be done, by the profession co-operating with the professional school, and I am equally convinced, that when the change is made, and the science and art of surgery are brought into proper perspective, much of our over-interference will seem as absurd to our successors, as the over-medication of our fathers in the earlier part of the 19th century seems to us.

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ARTICLE II.

The Shattuck Lecture.

CONCERNING DIABETES INSIPIDUS AND THE POLYURIAS OF HYPO-PHYSIAL ORIGIN.

By Harvey Cushing, M.D.,
of Boston.

Delivered June 10, 1913.

CONCERNING DIABETES INSIPIDUS AND THE POLYURIAS OF HYPO-PHYSIAL ORIGIN.

PITUITARY GLYCOSURIA.

IT has long been recognized that polyuria, with the appearance of dextrose in the urine — the typical symptomatic expression of diabetes mellitus, in other words — is a not infrequent accompaniment of acromegaly. The view is shared with my co-workers that this glycosuric manifestation of pituitary disease is indicative of the active stage of so-called hyperpituitarism, for in the advanced stages of acromegaly we have observed that the actual glycosuria or low assimilation limit for carbohydrates characterizing its early or recrudescent stages, usually becomes replaced by a high degree of sugar tolerance in which alimentary glycosuria can be provoked only by the ingestion of massive doses of sugar.

Certain experimental investigations with Goetsch and Jacobson[1] have shown (1) that experimental manipulations of the infundibular lobe cause a transient post-operative glycosuria, (2) that the injection of extracts of this lobe will cause glycosuria in well-fed animals, and (3) that after its surgical removal the animals acquire an increased tolerance for carbohydrates, accompanied by adiposity — an experimental condition comparable to the increased sugar tolerance shown by the clinical states of adiposo-genital dystrophy, which we therefore have come to recognize as expressions of pituitary insufficiency.

25

These findings offer experimental support to the view which we have advanced, that in the early glycosuric stages of acromegaly, in addition to the anterior lobe changes, an hyperplasia or functional activation of the posterior lobe occurs, which in the further progress of the disorder is often replaced by a relative functional insufficiency of this part of the gland.

Aware of the close chemical interrelation of the glands of internal secretion, we fully realize that the mellituria of hypophysial disease may indicate some secondary change in the pancreatic islets, though as yet histological evidence of this is lacking. We feel, however, that in the diabetic conditions under discussion the pituitary lesion is the primary factor, and this is supported, in negative fashion, by a series of observations with Jacobson, in which we have found that animals who have acquired a high sugar tolerance after extirpation of the posterior lobe may subsequently be deprived of the pancreas without the classical glycosuric consequences of the procedure described by Meyring and Minkowski.

PITUITARY POLYURIA.

It is, however, to the non-glycosuric form of pituitary diabetes that I wish on this occasion to call your particular attention, for this symptomatic expression of hypophysial disease has almost entirely escaped general recognition.

In a monograph written two years ago,[2] dealing with the clinical aspects of hypophysial derangements, comment was made on the fact that in certain cases polyuria and polydipsia may so dominate the clinical picture as to justify the designation of diabetes insipidus — a diagnosis which had actually been made, at one stage or another during the progress of the malady, in a number of the examples of dyspituitarism which were cited.

It was my intention, in conjunction with one of my assistants, Dr. Howard C. Naffziger, to make a detailed

report of our personal experiences in this direction during the past few years at the Johns Hopkins Hospital and to assemble the past clinical observations which had a bearing on the subject. This intent has been anticipated in large part by the publication, from Minkowski's clinic in Breslau, of an excellent article by E. Frank,[3] in the Berliner klinische Wochenschrift. This author, on the basis of a single personal observation — a case of bullet wound of the pituitary fossa — in conjunction with the available data from the literature, has taken an even stronger position in favor of the hypophysial relationship to diabetes insipidus than we might have ventured to assume. However, the matter is of sufficient general interest to justify, I trust, the bringing before you in this Shattuck Lecture of such facts as may be added to the data which others have accumulated.

EXPERIMENTAL OBSERVATIONS.

The discovery was made by Schäfer and Magnus in 1901 that extracts of the posterior lobe of the pituitary body possess diuretic properties of high degree, the reaction following their injection being a long-continued one, associated with an increase in volume of the kidney. Subsequently Schäfer and Herring pointed out (1906) that the renal arteries are exempt from the general constricting effect exercised by posterior lobe extracts upon other vascular channels and upon unstripped muscle in general. They expressed the belief, however, that the diuresis which they observed was the result of a direct action upon the renal epithelium and that it was independent of the hemodynamic response to the extract, for it persists long after the secondary fall in blood pressure and recession of the kidney to its original size.

In the course of our Baltimore studies in the Hunterian Laboratory (1908–12) it was noted that after certain experimental manipulations of the canine hypophysis a post-

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operative polyuria, often of some days' duration and at times reaching a tenfold increase over the normal output, was of frequent occurrence. In 1909 mention was made of these post-operative polyurias in an article by Crowe, Cushing and Homans,[4] dealing specifically with the effects of hypophysial transplantation, and in a subsequent paper by the same co-workers * the protocols of fifty examples of experimental hypophysectomy (Series of 1908–9) were given in tabular form.

It may be gathered from these tables that oliguria rather than diuresis followed a total extirpation in the adults, though in the younger animals which survived the loss of the gland for a longer time there was often a transient increase in the amount of urine for a day or two. On the other hand, in the series of partial extirpations in which the posterior and a portion of the anterior lobe were excised, post-operative polyuria was almost always observed, and this was also true of the animals deprived of the posterior lobe alone.

Control observations showed that no polyuria ensued if the operation was carried merely to the point of a free exposure of the gland, stopping short of the final step of actual tissue extirpation. This was construed as an argument against the assumption that the procedure served to excite some predicated diuretic and glycosuric center in the adjacent floor of the third ventricle, rather than that the manipulation of the gland itself provoked the diuresis.

In the series of operations carried out in the succeeding year (1909–10)[5] with Goetsch and Jacobson, although the experiments were reported from the standpoint of the glycosuric rather than the diuretic response, nevertheless

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* Experimental Hypophysectomy. Bull. Johns Hopkins Hosp., 1910, vol. xxi, pp. 127–169. A tentative opinion was expressed that we were dealing solely with an anterior lobe effect — an opinion shown to be erroneous by the observations of the following year.

the protocols show, in similar fashion, the usual non-appearance of polyuria after total extirpation (Fig. 1), whereas after a posterior lobe removal it was customary to observe a prompt post-operative increase in the urine, which occasion-
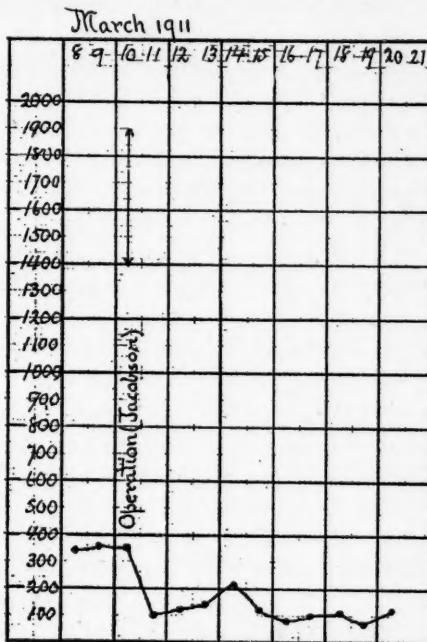
FIG. 1.

Chart showing post-operative oliguria after removal of practically the entire gland.

PROTOCOL. No. 16. Series 1910–11. 7.4 kilo. puppy. March 10: "Near total" hypophysectomy, including posterior lobe. Animal sacrificed for kymographic observations March 21.

ally reached an extraordinary figure for a dog, far in excess of the ingested fluids.

In the operative performances which served to induce hyperglycemia it was observed that the coincident diuretic effect of the procedure was more prolonged than the glyco-

suric response; and it was doubtless this extreme post-operative polyuria which in our earlier experiments led us to overlook the transient outpouring of sugar, so commonly noted in the second series, in which care was taken to examine the first voided specimen for the presence of a reducing substance.

We do not mean to imply that a diuretic response is invariable, but merely that it is commonly observed, and our further experiences, based on the more recent hypophysectomies conducted by Goetsch, Crowe or Jacobson during the past two years (1910–12), support the view that the clean-cut posterior lobe removals elicit polyuria with the greatest regularity. The accompanying three charts show this post-operative diuresis in its varying degrees: Fig. 2, in its extreme form with an immediate polyuria of high degree — almost four liters in the twenty-four hours, succeeded by a quick fall to the normal during the next day or two; Fig. 3, in less extreme form, the wave of polyuria being of somewhat longer duration; and Fig. 4, in what may be regarded as an average reaction for our posterior lobe removals.

These comparatively transient experimental reactions are chiefly of interest in showing the relation of the glandular manipulations and consequent secretory discharges to diuresis. More enduring polyurias, however, occurred in four of our experiments, all of them being instances in which the hypophysial stalk was purposefully divided or obstructed, leaving the otherwise intact gland, or a large part of it, *in situ*. In one of these animals (a 7 kilo. fox terrier which ultimately developed characteristic symptoms of hypopituitarism after a stalk separation, combined with a partial lateral removal of the anterior lobe) a polyuria varying from 675 to 1640 c.c. per diem, persisted for six months — a veritable diabetes insipidus of experimental origin (Fig. 5).
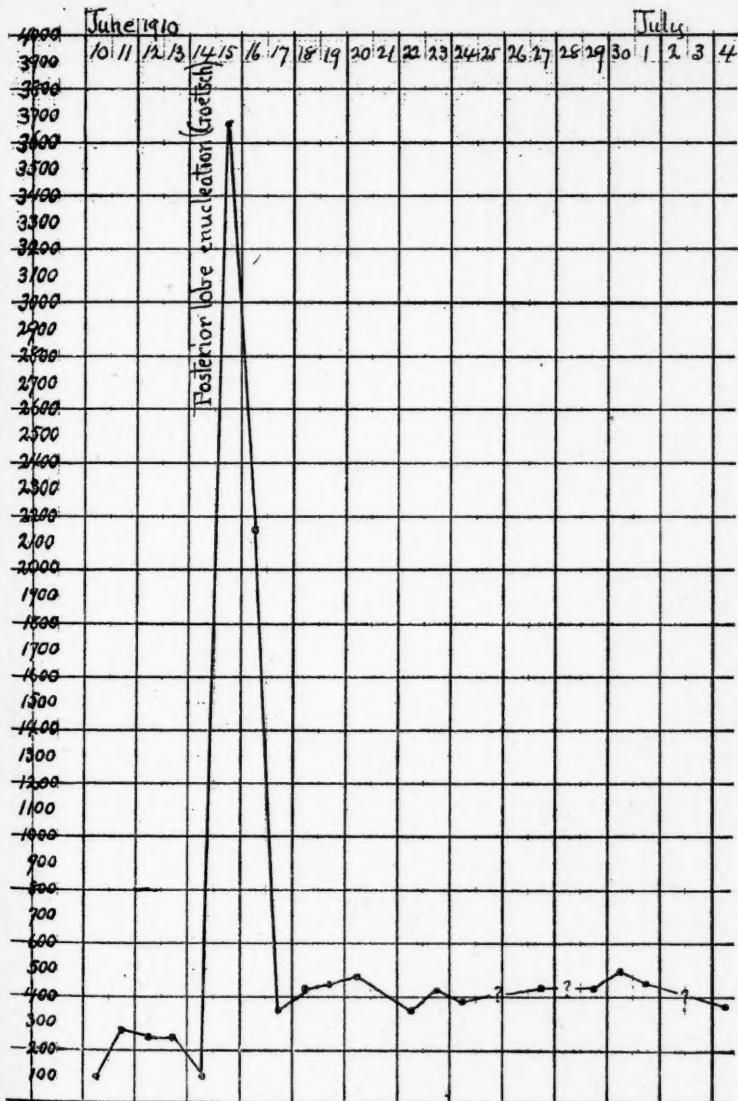
FIG. 2.

Chart showing extreme post-operative polyuria with excretion of 3700 c.c. in the first 24 hours; 2150 c.c. on the second day, with an abrupt fall to nearly the normal level.

PROTOCOL. No. 67. Series 1909–10. Seven kilo., 10 months' puppy. Posterior lobe extirpation.

Somewhat prolonged reactions were also observed in certain experiments in Crowe's series (1908–9) already re-
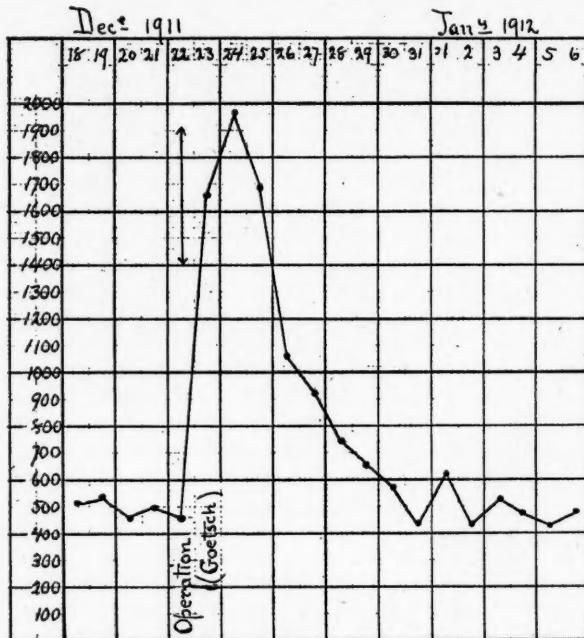
Fig. 3.

Chart showing moderately extreme transient polyuria.

PROTOCOL. 15.5 kilo. adult dog. Eck fistula performed Nov. 10, 1911. Animal kept in good condition on calcium dietary. On Dec. 22 a posterior lobe hyphophysectomy was performed, with the usual polyuria. No sugar present in the first voided specimen, which showed a lowered specific gravity of 1015, the previous and subsequent average being 1030.

A pancreatectomy was subsequently performed on this animal, without glycosuria. Neither the Eck fistula nor the pancreatic operation was followed by polyuria.

ferred to, in which we made an immediate subcortical transplant of the excised posterior lobe fragment — a measure having a certain experimental analogy to simple stalk separation, in view of the fact that the chief blood

supply of the gland passes into it by way of the infundibular attachment. In two of these animals (*e.g.* Fig. 6) the transplant was removed on the fifteenth and twelfth days re-
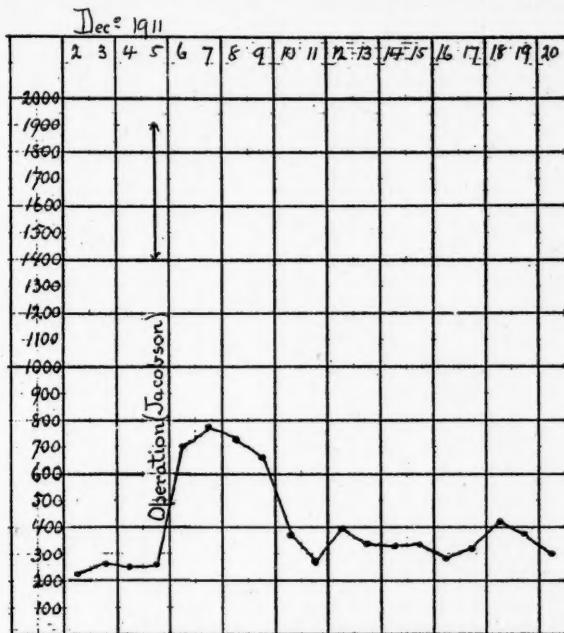
FIG. 4.

Chart showing the average moderate diuretic response after posterior lobe extirpation.

PROTOCOL. 6.5 kilo. puppy. Operation Dec. 5, with sugar (0.6 per cent. D.R.) showing on first specimen, despite the lowered specific gravity of 1012 from the preoperative specific gravity of 1028, due to the polyuria. Animal sacrificed for kymographic studies Dec. 20.

spectively, with prompt subsidence of the polyuria. In the third animal, on the other hand, the transplant was not removed and the polyuria continued (Fig. 7) until the dog was sacrificed on the twenty-fourth day in order to observe the histological condition of the implanted tissue, which was thought to be viable.
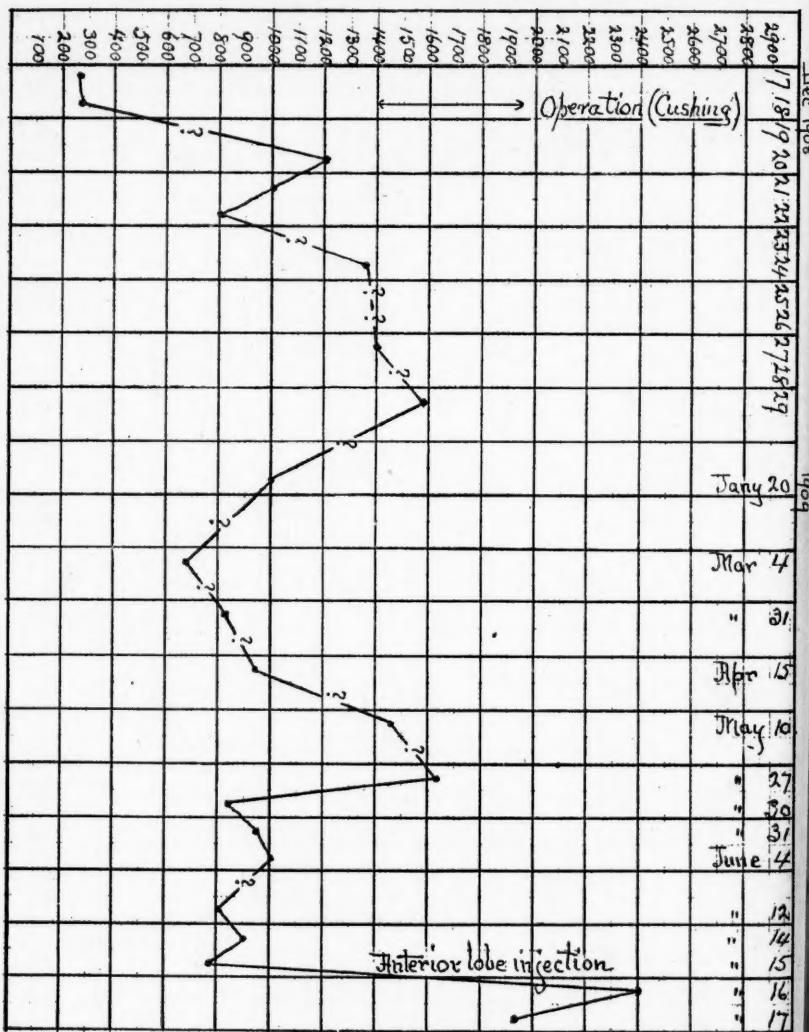
Fig. 5.

Chart showing polyuria prolonged over a period of six months after hypophysial stalk separation. PROTOCOL. Seven kilo. fox-terrier. Dec. 18: Stalk separation with fragmentary anterior lobe removal. Polyuria observed on the six observations during the succeeding ten days and on all occasions when the amount was measured during the succeeding six months, the animal meanwhile acquiring the characteristic adiposity with drowsiness, subnormal temperature and so on, of hypophysial insufficiency. A marked increase of polyuria followed the injection, on June 14, of 10 c.c. of a one per cent solution of anterior lobe emulsion of bovine gland. Animal sacrificed on June 17.

Schäfer[6] in the course of some experiments on the effect of glandular transplants in non-hypophysectomized animals, observed that the subcutaneous implantation of the pos-
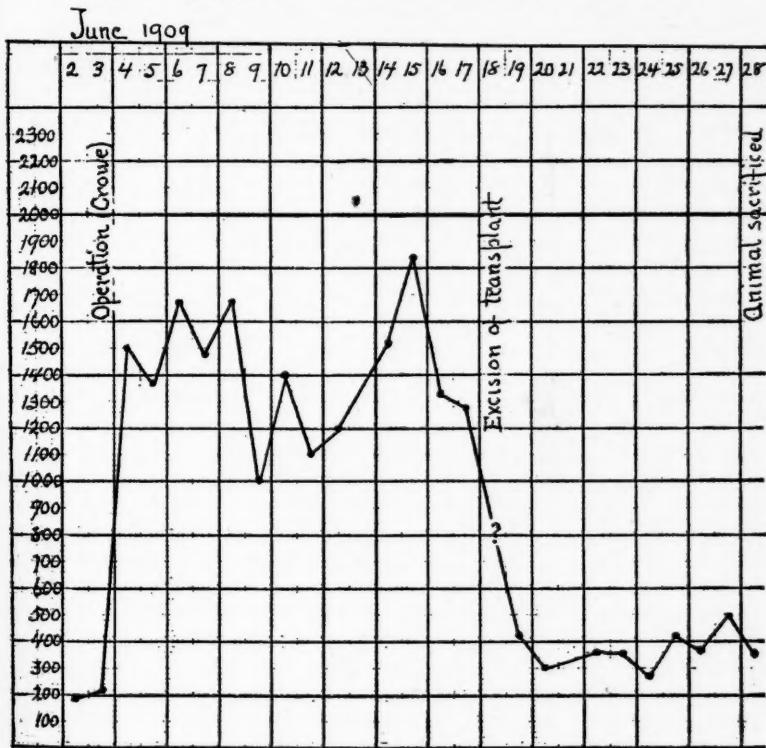
FIG. 6.

Chart showing persistent polyuria following posterior lobe reimplantation in the cerebral subcortex after excision. Polyuria promptly interrupted after excision of the transplant on the fifteenth day.

terior lobe from one animal to another causes a transient polyuria, which subsides in a few days, coincident presumably with the absorption of the secretory products contained in the implanted tissue. It would appear, moreover,

from certain observations made by Stiles, under Schäfer's direction, that the posterior lobe substance given by mouth
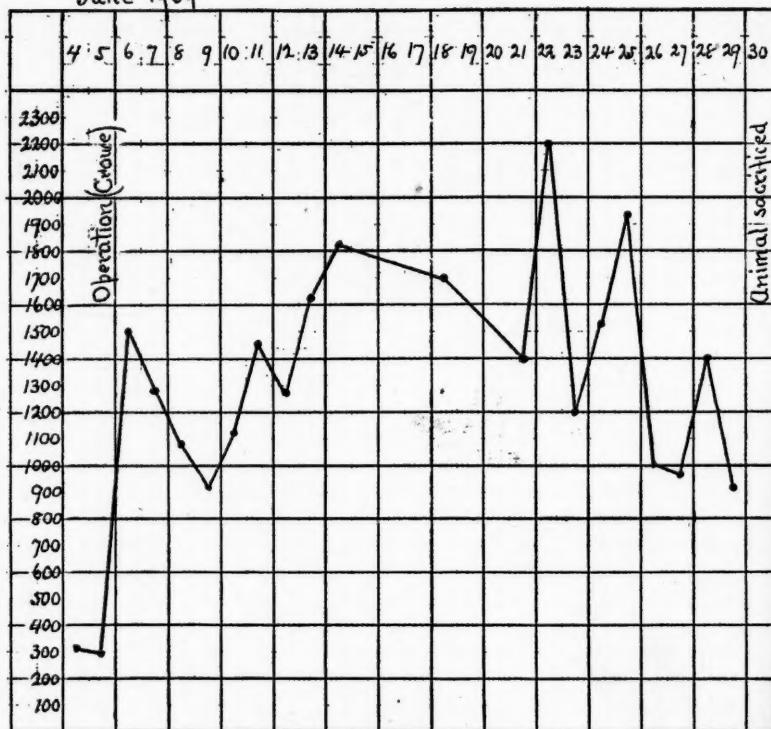
FIG. 7.

Chart showing persistent polyuria following posterior lobe reimplantation in the cerebral subcortex. On all occasions during the twenty-five days following the operation, when the 24-hour amounts were measured they varied between 900 and 2200 c.c.

increases urinary output, and thus promises to be of clinical value as a diuretic. This observation also conforms with our own experiences with the oral administration of extracts.

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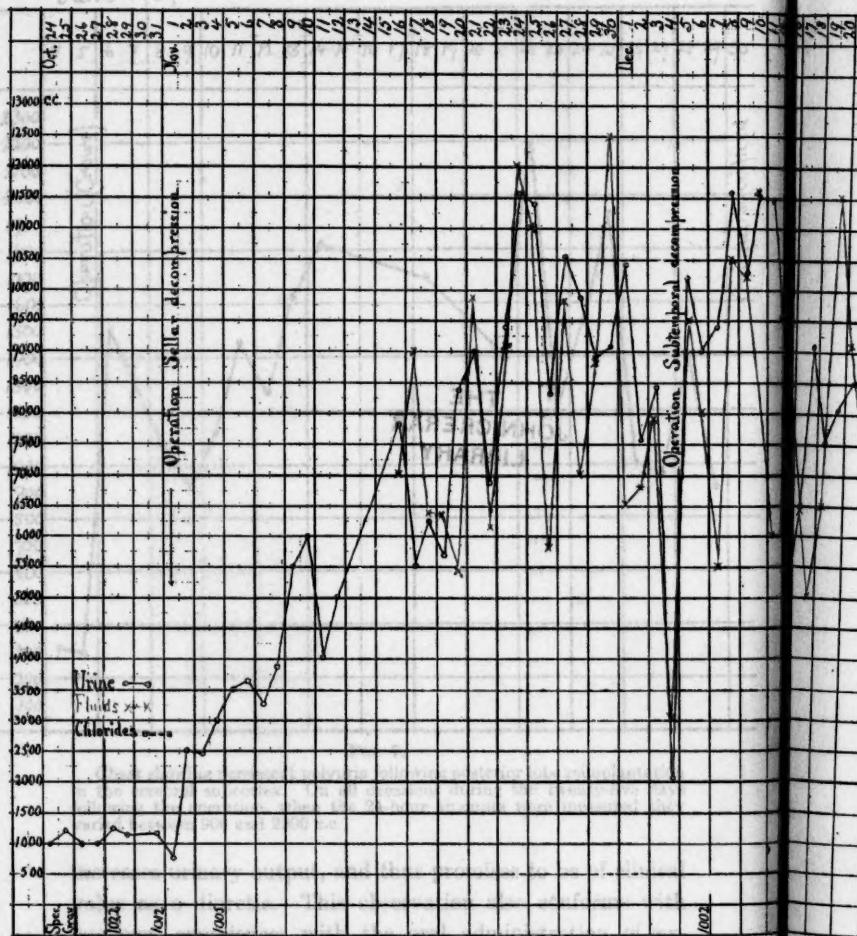
Chart showing a three-months' wave of polydipsia and polyuria follow... of the floor
water in red; estimated ch... January 6th

Fig. 8.

...llowing of the floor of the pituitary fossa. Urine in solid black line; ingested ...d chl... January 6th in broken line.

The experimental polyurias heretofore cited have been brought about either by a direct hypophysial injury, by the injection of extracts, or by glandular implantations. An hypophysial diuresis, however, may be elicited in still another way, namely, by nerve stimulation. In some recently recorded observations in collaboration with Weed and Jacobson[7] on the autonomic control of the gland, the chief argument for the passage of nervous impulses from the medulla through the cord to the three upper thoracic nerves and thence to the pituitary gland by way of the cervical sympathetic relays, lay in the elicitation of glycosuria from stimuli applied to this pathway. During the course of these studies, however, we commonly observed, coincident with the glycosuric response, an abundant outpouring of urine of low specific gravity; a rabbit, for example, would often excrete 15 or 20 c.c. in a very few minutes, and at times as much as 150 c.c. in the course of a few hours after stimulation of the superior cervical ganglion. A similar prompt and often excessive diuresis, provoked by the intravenous injection of concentrated cerebrospinal fluid in small amounts, was one of the facts advanced by Goetsch and myself[8] in favor of our contention that the posterior lobe secretion finds its way into the cerebrospinal fluid. These matters are of interest in connection with the subject of emotional or neurogenic polyurias, the further discussion of which at this time would lead us too far afield.

Despite the suggestiveness of many of these laboratory observations it must, nevertheless be acknowledged that a long-continued polyuria of high degree, comparable to the clinical conditions of diabetes insipidus, has hardly ever been observed, though in a number of cases, after posterior lobe extirpation, animals whose pre-operative average output was *circa* 300 c.c., continued to excrete an amount two or three times as great (*circa* 700 c.c.) for the succeeding month or two.

In summarizing the experimental data it may be said that:

(1) The infundibular lobe contains, in addition to the substance capable of glycogenolysis, a chemical body or hormon capable of eliciting diuresis.

(2) Under certain operative conditions which entail posterior lobe manipulations there often occurs a diuretic response, and occasionally an extreme polyuria, whereas a temporary diminution in the excreted urine is apt to follow other operative procedures, requiring an equally long anesthetization.

(3) Posterior lobe implants may cause a temporary polyuria, which subsides on the removal of the implanted tissue.

(4) Stimulation of the autonomic system of nerves to the gland elicits diuresis.

(5) Certain operative procedures, such as separation of the infundibular stalk, and occasionally a simple posterior lobe excision, may call forth a somewhat prolonged polyuria.*

* It will be apparent to all that there exists a discrepancy in these diuretic reactions which does not apply to those accompanied by glycosuria. For in the case of the pituitary glycosurias the administration of extracts, direct glandular stimulation, or stimulation of the autonomic nerve supply to the gland, all produce glycosuria, which is recognized as an expression of glandular hyperplasia in clinical cases; whereas experimental extirpation of the gland leads to the reverse condition, namely an increased tolerance for carbohydrates, just as in clinical states an increased sugar tolerance coincides with the glandular insufficiency brought about by injury or compression by a tumor.

In regard to the diuretic response, on the other hand, though the administration of extracts, direct glandular stimulation or stimulation of the autonomic nerve supply are likewise capable of eliciting polyuria, nevertheless the experimental extirpation does not lead to the reverse of polyuria, nor in the clinical states with evident posterior lobe insufficiency do we find a diminished urinary output. On the contrary, active polyuria is not infrequently seen in clinical cases of hypopituitarism associated with a high sugar tolerance.

Thus hypophysial glycosuria and polyuria do not go hand in hand. Explanations for this apparent discrepancy will doubtless be afforded by future studies.

CLINICAL OBSERVATIONS.

Diabetes insipidus, according to our best known texts, is symptomatically defined as a long-continued disorder characterized by polyuria and polydipsia, with a sugar-free urine of low specific gravity. Two varieties of the malady are commonly recognized: the so-called *idiopathic* form, supposedly originating in the kidneys, is sharply distinguished from a *symptomatic form*, which includes not only the polyurias shown by supposedly psychopathic or hysterical individuals, but also those provoked by some emotional insult, as well as those for which there may be an actual organic neurological basis, such as cerebral trauma, syphilis or tumor.

Meyer, in 1905, considered the idiopathic form to be a primary renal polyuria due to a functional disability of the kidneys which rendered them incapable of secreting urine above a certain low specific gravity, on which basis the ingestion of salt should fail to concentrate the urine and thus should serve to distinguish true diabetes insipidus from the condition brought about by a primary polydipsia. It is held, moreover, that in cases of true diabetes insipidus deprivation of water does not check the polyuria, and some have claimed that the excretion of ingested fluids is more rapid than normal (tachyuria); and this is advanced in support of the view that the disorder is a primary polyuria rather than a primary polydipsia. Others contend that the opposite condition, namely bradyuria, exists, and indeed on etiological grounds the subject is in a state of great confusion.

As will be recalled, Claude Bernard observed, fifty years ago (1854-55), that a transient glycosuria could be provoked by a piqûre at a point in the floor of the fourth ventricle between the origin of the pneumogastric and auditory pairs of nerves, and also that stimulation of a point just anterior to this so-called sugar center would occasionally

produce a transient polyuria without the coincident appearance of sugar in the urine. It is natural that many have assumed the existence of some relationship between these experimental glycosuric and diuretic piqûres and certain clinical glycosurias and polyurias, particularly those of a supposedly emotional or neurogenic origin. I do not believe, however, that these conditions, so often precipitated by cerebral trauma, whether psychic or mechanical, were capable of interpretation until it was shown, in collaboration with Weed and Jacobson,[9] that impulses which pass from Bernard's centers by way of the cervical sympathetic are capable of discharging from the gland a glycogenolytic as well as a diuretic substance.

. In our somewhat extensive experience with patients who have received traumatic injuries involving the cranial base, a pronounced and enduring polyuria with polydipsia has been observed in a number of instances; and similar conditions have been reported by others. I have pointed out elsewhere that in basal fractures, even though the fissures may not actually run through the sella turcica, the pituitary body is often the seat of extravasation, which may readily account for the diuretic and glycosuric response occasionally exhibited by the recipients of severe cranial injuries. In one such individual under my care a year ago, there was intense polydipsia, with an average daily output of about 8 liters of sugar-free urine with a low specific gravity, the condition persisting for the six weeks the patient was under observation in the hospital. As was true of the experimental conditions heretofore described, so also in these cases of basilar fracture, when a glycosuric response occurs it is apt to be transient and the presence of sugar may be overlooked unless the first voided specimen is secured, whereas the polyuria is commonly of much longer duration.

Though as eminent an authority as Van Noorden is skeptical of the possibility that a true diabetes may be thus

inaugurated by trauma, a number of striking cases have been
recorded by Abt and Strauss, by Wieland, by Nothnagel
and by Naunyn and Lepine. In view of these authentic
clinical examples and in the light of our laboratory ex-
periences, which bring a new element into the discussion,
namely the hypophysial secretion, it seems safe to conclude
that a suitable injury, affecting the infundibular lobe with-
out obvious lesion of any nerve center, may set up a pro-
longed polyuria, justifying the designation of diabetes
insipidus.

Let us turn from this brief consideration of the traumatic
polyurias to those associated with some obvious process of
disease.

A review of the clinical histories included in many of the
past articles upon diabetes insipidus makes it clear that a
large percentage of the patients have shown symptomatic
evidence of a lesion involving the base of the brain, a gum-
matous meningitis affecting the structures in the middle
cerebral fossa being a particularly common accompaniment
of the disorder.   This was true of several of Futcher's cases
gathered from the Johns Hopkins Hospital records,[10] and
one of his patients, subsequently under my own observa-
tion, showed characteristic neighborhood manifestations of
an hypophysial lesion coupled with signs of glandular in-
sufficiency.

The fact that tumors or other lesions in the neighbor-
hood of Bernard's center are far less likely to be accom-
panied by polyuria and glycosuria than are similar lesions
situated farther forward in the interpeduncular region, has
long been a source of confusion, and some have even gone
so far as to predicate so-called diuretic and sugar centers in
the floor of the third ventricle.   An observation of particular
significance in this connection was commented on by Futcher
and has been recently emphasized again by E. Frank, namely
the surprising frequency with which primary optic atrophy,

often with bitemporal hemianopsia, accompanies the encephalitic polyurias often classified as diabetes insipidus *; indeed, the diabetes has even been looked upon by some as a cause of the optic atrophy.

As stated in my introductory paragraphs, in our considerable experience with hypophysial disorders a surprising number of the patients had either been regarded as the victims of the malady under discussion at one time or another, according to their own clinical story, or else the condition was apparent during their hospital residence. In most of these individuals the existence of a pituitary involvement was sufficiently clear, in view of the coincident local manifestations of tumor, though we are becoming familiar enough with these clinical states to recognize the evidences of dispituitarism in the absence of these telltale neighborhood signs.

However, from a critical standpoint unequivocal proof comes only through post-mortem examinations, and of these there have been a sufficient number recorded in the literature, supplemented by the evidence of our own series of cases to make a strong brief.

Several of these cases have been brought together by E. Frank; for example, a tubercle of the infundibulum reported by Hagenbach in 1882, a sarcoma of the hypophysis by Rosenhaupt in 1903, a cystic tumor below the third ventricle by Finkelnburg in 1910, and two examples of gummatous involvement of the infundibular region, both with bitemporal hemianopsia and diabetes insipidus, have been put on record by Oppenheim. Though not certified by

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* According to E. Frank, Kruse in 1894 reported 35 cases of bitemporal hemianopsia, 7 of them showing diabetes insipidus. Spanbock and Steinhaus in 1898 reported 50 cases of hemianopsia, 11 of them showing diabetes insipidus. Oppenheim has recorded one or two cases in which the post-mortem findings showed a gummatous meningitis, the medulla and pons being unaffected by the process.

autopsy, the situation of the lesion in many other reported cases has been reasonably definite, as was true of Frank's case — a patient who had received a bullet wound involving the pituitary fossa, with subsequent development of diabetes insipidus accompanied by adiposity and other symptoms indicative of a state of hypopituitarism.

Since the appearance of Frank's paper another example, certified by autopsy, has been recorded by Professor Simmonds of Hamburg.[11] The patient was a woman of 37, in whom an intense polyuria developed some months after an operation for cancer of the breast, the amount of urine fluctuating between 10 and 19 liters per diem. The autopsy disclosed a small metastatic nodule of the growth which involved the dorsum sellae, the posterior lobe and hypophysial stalk, the pars intermedia and pars anterior remaining free. A somewhat comparable condition occurred in the case of a patient who was under my care a year ago in Professor Halsted's service in Baltimore.

A young man, 22 years of age, entered the hospital January 24, 1912, *in extremis*, with a recurrent lymphosarcoma of the neck and metastases in the cranial bones. Aside from the local disturbances caused by the inoperable tumor his chief symptoms were an insatiable thirst and polyuria. Until shortly before his death, which occurred a month after his entrance, the daily amount of urine varied between 10 and 12 liters.

At autopsy a discrete nodule of the widely infiltrating growth was found by Dr. Whipple occupying the thickened stalk of the pituitary body. The kidneys were histologically normal.

In our series of something over 100 examples of primary hypophysial disease which have been carefully investigated, though many of them, particularly of the group showing hypophysial insufficiency, have shown polyuria, in six a condition existed which justified the clinical designation of diabetes insipidus, and in five of these individuals this had been one of the various clinical diagnoses advanced before admission. The following curtailed history will serve in illustration:

On November 23, 1911, J. B., aged 48, entered the Johns Hopkins Hospital, nearly blind, in a stuporous condition and utterly disoriented.

According to the history, he had received, six years before, a frontal injury which had fractured his nose. He subsequently suffered from headaches, occasionally accompanied by nausea and vomiting. He became forgetful, had periods of somnolence and lost his *potentio sexualis*. He acquired an enormous appetite, and polydipsia with extreme polyuria developed. His vision began to fail, and nine months before his admission a bitemporal hemianopsia was observed. Periods of diplopia followed. Owing to the polyuria several of his many attendants had agreed upon a diagnosis of diabetes insipidus.

On examination the case proved to be a typical one of hypopituitarism with outspoken and characteristic neighborhood symptoms, though the x-ray of the sella showed normal outlines.

The body temperature was usually subnormal, often registering as low as 96; the pulse was slow, often 60; and the respiration also was greatly slowed, with occasional rhythmicities of the Cheyne-Stokes type.

Somnolence was one of the most striking features, and as there were frequent periods of incontinence it was not always possible during his drowsy periods to collect the full 24-hours urinary excretion. At other times, when he was wakeful and responsive and the urine could be measured, the amount was always over 5 liters, not infrequently exceeding the ingested fluids.

Though the urine from time to time contained a trace of albumen and an occasional hyaline cast was present, there was no clinical evidence of arteriosclerosis, the blood pressure almost invariably registered below 100, and functional tests of the kidneys gave normal reactions.

He was under observation for five months, and during this time efforts were made to compensate for his glandular deficiency by the administration of extracts and by pituitary implantations, with but variable success. He ultimately died from an inhalation pneumonia on April 29, 1912.

The autopsy disclosed an interpeduncular cystic tumor — the usual squamous epithelial lesion derived from an anlage of Rathke's pouch. The hypophysis was greatly flattened and contained but a few normal cellular elements. The kidneys were histologically normal. There was no arteriosclerosis.

This is a fair example of the five other cases in which the polyuria was sufficiently pronounced to justify particular study. It is, moreover, the only one of the six in which occasional traces of albumen and renal elements appeared in the urine, and I may add in this connection that none of the patients showed evidences of arteriosclerotic changes, that

a persistently low blood pressure was commonly observed, and that standard functional tests of the kidneys gave normal reactions in the three patients in whom these tests were made.

Suggestive as the foregoing examples of spontaneous polyuria prove to be, there is still another case in the clinical series which is even more illuminating. In this patient an enduring polyuria was inaugurated by a transphenoidal hypophysial operation — an experience which is somewhat comparable, as will be observed, to the experimental consequences of hypophysial manipulations discussed in the first section of this paper. The story deserves a somewhat detailed recital.

Pituitary tumor with blindness from primary optic atrophy. Symptoms of hypopituitarism. Sellar decompression, provoking a post-operative diabetes insipidus.

Mrs. F. L., 40 years of age, entered the J. H. H., October 23, 1911, with the complaint of blindness and headaches.

There was nothing noteworthy in her family or past personal history, though from childhood she had suffered more or less from cephalalgia. Her adolescence was somewhat tardy, for her catamenia, though subsequently regular, did not begin until she was 16. She married at 20, and raised a family of six healthy children, the eldest 18 years, the youngest three months of age. In four other pregnancies she miscarried.

Present Illness. After her fifth confinement, four years before admission, she began to suffer from throbbing headaches, and a few months later failure of vision was first observed. This condition progressed, and in the course of the next two years she became almost completely blind.

Subsequently her sense of taste and smell became affected, and there were occasional uncinate gyrus seizures preceded by a dreamy state with an olfactory aura (as of something scorched, as bread, rubber or meat), and followed, in the more severe attacks, by a convulsion with loss of consciousness. Of late there had been some failure of memory with depression; also marked drowsiness.

Physical Examination. A well-nourished woman, 5 feet 6 inches in height, and weighing 150 pounds. Visceral (abdominal, thoracic, etc.) examination negative. Urine normal. Blood examination (including Wassermann test) negative except for an eosinophilia of 4 per cent; blood pressure averaged 110 mm. of Hg. No positive neurological signs aside from those of the pituitary neighborhood.

Analysis of Hypophysial Symptoms. (1) *Neighborhood:* The cranial x-ray disclosed completely obliterated sellar outlines. *Eyes.* Pupils dilated (7 mm.); sluggish reaction to bright light. Bilateral primary optic atrophy. Blindness so nearly complete that accurate perimetry was precluded though shadows of large moving objects were at times indistinctly made out in the nasal fields. Pupillary reactions also appeared to be better from a ray of light cast on the temporal than on the nasal retina — presumably the last stage of a bitemporal hemianopsia. Complete anosmia. Uncinate gyrus seizures as recorded.

2. *General Pressure Symptoms:* Headaches, extreme and paroxysmal and occasionally accompanied by nausea and vomiting. Some evidence of new tissue formation in the atropic nerve heads, with obscuration of the margins and of the lamina cribrosa.

3. *Glandular:* No skeletal change: no especial adiposity; no cutaneous change. Moderate hypotrichosis. Sugar assimilation limit 200 grams of levulose. Constipation marked. No polyuria or polydipsia. Pulse, temperature and blood pressure tended to be subnormal. Marked drowsiness. Other ductless glands negative.

November 1. Sellar decompression by transphenoidal route. The thin, bulging floor of the sella was easily removed in one large scale. The dura was incised, but instead of the expected soft struma a dense tissue mass was encountered. This was taken to be the flattened gland interposed between the operative field and the tumor. (A minute fragment of the tissue, removed for examination, subsequently showed flattened anterior lobe cells with a great increase of interstitial tissue.)

There were no surgical complications: no subsequent nasal discharge.

On recovering from the operation the patient exhibited a degree of thirst, which proved to be insatiable by the usual ward delivery of water. Not, however, until several days later did the associated polyuria become so marked as to attract especial attention (Fig. 8). Unfortunately there had been no test for sugar on the first specimen voided after the operation, though, according to the ward routine for all suspected hypophysial cases, the 24-hour amounts were recorded, except on three days (November 13 to 15 inclusive) when some specimens were lost. After November 16 the fluid intake and output were both measured.

As the poor woman's pressure headaches continued unabated, recourse was had, a month later, to a palliative subtemporal decompression.

December 4. Right subtemporal decompression A tense temporal lobe was disclosed. Uncomplicated healing. There was prompt and permanent relief from headaches but the polyuria, anosmia and subjective olfactory seizures continued as before and, as was anticipated, no improvement occurred in vision.

Observation on the Polyuria. (Fig. 8.) As stated, the sellar decompression of November 1 served to inaugurate an active polydipsia with polyuria. The primary wave of polyuria shown

in the accompanying chart persisted for three months, the 24-hour amount of urine reaching nearly 12 liters at the crest of the wave. The polydipsia was proportionate, and though from the plotted curve it would appear that the average fluid intake was less than the renal output, the ingested water only was measured. There were, however, many days when the excretion unquestionably exceeded the ingested fluids. However, her weight during these three months varied but slightly, at the lowest being 147.5 pounds, and on February 1, at the end of the primary period of extreme polyuria shown in the chart it was again at 150, her weight on admission.

Her thirst was unquenchable and was most distressing to observe. A two-liter jar of water which siphoned to her mouth, was kept at the head of the bed, and the poor blind creature almost continuously sucked at the tube, except during her sleeping hours. It was often necessary to refill the jar every few hours.

The chart shows that only on the day of the second operation (December 4) was there a marked break in the polyuria, owing doubtless to a diminished intake and possibly, too, to the fact that some specimens may have been lost in the operating room.

At no time were there any renal elements, sugar or albumin, acetone or diacetic acid in the urine.

Functional tests of the kidneys at the height of the polyuria showed no alteration from the normal. The phenolsulphonephthalein test for tubular function showed a positive reaction in 4½ minutes, and 47 per cent was returned in the first hour. Tests with potassium iodide, with carbol-fuchsin and with lactose all gave normal results, and the glycosuric reaction to phloridzin was likewise normal.

The specific gravity of the urine throughout the three months averaged from 1005 to 1006. Practically the lowest registration, namely 1002.5, occurred on the first two days following the inauguration of a period of salt-free diet, though at this time the polyuria was not at its extreme height. Attempts to increase the urinary concentration by administering NaCl were obscured, owing to the impossibility of keeping the ingested fluids low enough for the urine to be appreciably affected by any reasonable amount of salt.

On February 1, sugar and salt were withdrawn from the dietary and the liquids were limited to 2200 c.c., with resultant rise in the specific gravity; on the first two days the excretion exceeded the ingested fluids. The restriction of liquids, however, caused so much distress that prolonged observations were unjustifiable, and at this time, moreover, there was an evident spontaneous lowering of the degree of polyuria which had preceded.

She remained in the hospital through the month of February, during which time the polydipsia moderated considerably. On some occasions the 24-hour amount of urine fell almost to normal limits. She was discharged on February 24, 1912, four months after her admission. Since her discharge frequent reports of her condition have been received through her physician. There has been an occasional slight wave of thirst with polyuria amounting

to three or four liters in the 24 hours, but for the most part the amount ranges around the normal.

She continues (April, 1913) to be free from her former pressure headaches, though her uncinate gyrus seizures still recur and her blindness and drowsiness remain about as before.

'Tis an ill wind, indeed, that blows no benefits, and the experience with this unfortunate patient, who presented a therapeutic problem for which we have as yet no satisfactory surgical or other solution — the presence of an interpeduncular growth, which flattens and functionally obstructs the underlying pituitary gland — at least has added something to our knowledge of an obscure malady.

Though it may not be clear in just what way the manipulation of the compressed gland served to inaugurate the polyuria, the experience offers a strong argument in favor of the view that an actual disturbance of the pituitary body itself, rather than the stimulation of some predicated diuretic center in the remote third ventricle surmounting the growth, was the inciting cause of a condition worthy of the designation of diabetes insipidus.

It may be said in conclusion that certain clinical observations, coupled with the experimental data which have been assembled, suggest not only that,

The emotional polyurias are in all likelihood the expression of a neurogenic discharge of hypophysial secretion, but also that,

The clinical polyurias of longer duration are in many instances merely the symptomatic expression of an internal secretory disturbance brought about by injury or disease involving the hypophysial neighborhood.

Hence, whether or not there actually proves to be a form of polyuria of primary renal origin, our present conceptions of so-called diabetes insipidus need to be recast, with especial reference to the factor of the secretory activity of the pituitary body and particularly of its posterior lobe.

NOTE. — Since the preparation of this paper an interesting communication under the title "Diabète insipide avec infantilisme," made by Peirre Marie and Boutier before the Société de Neurologie de Paris, has been published in the Revue Neurologique, 1913, vol. xxi, pp. 555-560. The case in all likelihood was one of infantilism associated with an hypophysial lesion, though no radiographic observations were made.

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THE MODE OF TRANSMISSION OF POLIOMYELITIS.

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THE MODE OF TRANSMISSION OF POLIOMYELITIS.

From a practical standpoint the mode of transmission is the most useful single factor in combatting a disease. The health officer would prefer to know the precise mode or modes of transmission of any disease rather than its cause, or pathologic anatomy, or even its treatment. Hence a large amount of work has been done to determine how the virus of poliomyelitis leaves the body, how it enters its victim, and the route it takes from one person to the next. Despite all the thought and work that has been focused upon this problem, the mode of transmission of poliomyelitis remains an open chapter, and although much light has been thrown upon the subject, the present state of our knowledge does not permit of dogmatic, much less final statements.

There are two avenues of approach to a problem of this sort; one, through epidemiological field studies, and the other through laboratory research work. Both these trails have been blazed. Much of the epidemiological work has given conflicting results, and much of the laboratory work has likewise been confusing. The evidence obtained from the field and that from the laboratory, however, do not have an equal standing before the court. The fallibility of epidemiological evidence has long been recognized. Sanitarians who have had a long experience know full well that it has always been necessary to revise the chapter on the epidemiology of a disease as soon as its mode of transference is discovered. All those who have collected field data are fully aware of the pitfalls. Errors are unavoidable from the very nature of the circumstances; the personal equation and also the limitations of the investigator often warp

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or dwarf the important facts.   In any event, the enormous
mass of data collected by careful investigators in the field
is perplexing and difficult to analyze.   Even if the epi-
demiologist has the detective instinct of a Sherlock Holmes,
and the statistical genius of a Karl Pearson, he may be
wholly carried off the track by the missed cases, and by the
carriers, or by an incomplete knowledge of unusual forms of
the disease, or by unknown factors in its etiology.   On the·
other hand, the exact observations from the laboratory
often throw a flood of light upon our field work, and when
the two are correlated we have real and useful additions to
our knowledge.

There are many theories to account for the spread of
poliomyelitis.   The chief ones may be summarized under
four headings: (1) that it is a "contagious" disease, com-
municated directly from person to person through the
secretions from the mouth and nose; (2) that it is an insect-
borne disease; (3) that it is conveyed through dust; (4) that
it is an alimentary infection, the virus being taken in with
food and drink and absorbed from the digestive tube.   There
is evidence from the field and from the laboratory to sup-
port each one of these theories.   These four theories, how-
ever, do not include all the views brought forward to ex-
plain the mode of transmission of infantile paralysis.   For
example, the hypothesis has been expressed that the disease
is transmitted to man from lower animals particularly
domesticated animals, but there has been no convincing
demonstration that the infection occurs naturally in any
other animal than man.

In view of the uncertainty concerning the mode of trans-
mission of poliomyelitis it is worth while to take stock of
our knowledge of this subject.   I have therefore briefly
summarized the evidence pro and con.

That anterior poliomyelitis may be a contagious disease
was first announced by Wickman of Sweden whose epi-

demiological investigations upon the subject are now classic. Wickman formulated a new symtomatology; his greatest contribution to the subject was perhaps the discovery that abortive cases of the disease occur. These mild, and hitherto unrecognized clinical forms, shed an entirely different light upon the epidemiology. Wickman brought forward strong evidence in support of the view that the disease was transmitted directly from person to person, especially through the abortive or missed cases, as well as through suspected carriers.

The theory that infantile paralysis is a "contagious" disease was the first, and is the most natural, explanation to account for its spread. In many respects infantile paralysis resembles epidemic cerebrospinal meningitis, with which disease it is, in fact, sometimes confused. Flexner has emphasized the resemblance between the two infections, and has been an able and valient champion of the view that the virus in both these diseases leaves the body in the secretion from the mouth and nose and enters the victim through the same channel. Corroboration of this view has come especially through the work of the Swedish investigators, Kling, Pettersson, and Wernstedt who claim to have demonstrated the virus in the secretions from the nose and throat, not only in cases during the acute stage, but during various stages of convalescence, and even in healthy carriers. Furthermore, Osgood and Lucas demonstrated the virus in the mucous membrane of a monkey $5\frac{1}{2}$ months after recovery from the experimental disease and recently they recovered it from a chronic carrier in man. Kling claims to have found the virus in the nasopharynx up to seven months in a few human cases. Finally, it is possible to infect monkeys simply by placing the virus upon the uninjured mucous membrane of the nose and throat. The evidence, therefore, that we are dealing with an infection that leaves the body in the secretions from the nose and

throat, and enters by the same channel, is strong, both from epidemiological studies and from laboratory investigations. That this evidence, however, is not conclusive, may be gleaned by a little closer consideration of the facts.

It is important first of all to remember that we have no clear-cut criterion by which to judge what is and what is not anterior poliomyelitis. When the symptoms are characteristic and the lesions typical we are justified in making a definite diagnosis. In any critical case, however, further corroboration must be had by transferring the virus from monkey to monkey in order to demonstrate that we are, in fact, dealing with a communicable infection capable of reproducing itself. When we apply this criterion to some of the work that has been reported, to support the view that infantile paralysis is a "contagious" disease, we find the evidence not as strong as the conclusions of the experimenters would lead us to suspect. The mere fact that an animal has an acute paralytic affection, associated with perivascular infiltrations, degeneration of the neurons, and occasional hemorrhages into the cord, is not enough, in the present state of our knowledge, to justify us in labeling it poliomyelitis. The criterion in critical cases must be the power of the virus to reproduce itself and repeat the symptoms and lesions of the infection through succeeding generations.

There has been a long series of negative results in attempts to demonstrate the presence of the virus in the secretions from the mouth and nose. Strauss, Rosenau, Sheppard and Amoss, Flexner, and also Anderson, and others, have all reported failures in this regard. These negative results have a certain degree of positive significance, for if the usual means of transmission of the disease is through the secretions from the mouth and nose we should not have such great difficulty in demonstrating its presence

in these secretions. Only Kling,* Pettersson and Wernstedt have found it comparatively easy to make this demonstration. These investigators believe that they have established the important fact that carriers occur, and are several times more numerous than the frank and abortive cases of poliomyelitis combined. Yet Flexner, Clark and Frazer report only one positive result out of numerous trials. They succeeded in demonstrating the virus of poliomyelitis in the washings from the nasopharynges of the parents of a child suffering with poliomyelitis. The parents, however, showed no symptoms of illness.

The virus of anterior poliomyelitis is widely diffused throughout the body. It has been found in greatest virulence and concentration in the spinal cord of infected persons and animals. The virus is also quite constantly present in the brain and other organs and tissues as, for instance, the mucous membrane of the nose and pharynx, the mesenteric glands, the axillary and inguinal lymph nodes, and even in the blood and the cerebrospinal fluid. Recently the virus has been demonstrated in the mucosa of the intestinal tract, and finally in the feces. It is therefore no surprise that a virus with such a wide distribution and so generally diffused throughout the body may occasionally be found in the secretions from the nose and throat. These facts make us hesitate to conclude that infantile paralysis

* Kling found it comparatively easy to demonstrate the presence of the virus in the washings from the mucous membranes. Thus he found that 78 per cent of the monkeys contracted the disease after inoculation with water in which the mucous membranes of poliomyelitis cadavers had been rinsed. The virus was also found almost constantly in the secretions from the nose and throat of acute poliomyelitis patients. These results are so much at variance with the results obtained by American investigators that the question has arisen whether we are dealing with the same virus in America as that found in Sweden, or whether the virus has marked differences in virulence, or whether there is some experimental error or more likely, an incorrect interpretation of results.

must be a contagious disease, simply because it has been
demonstrated experimentally that the virus may be found
occasionally in the secretions from the nose and throat; it
would be just as logical to conclude that the disease in its
spread resembles typhoid fever because the virus has been
demonstrated in the mucous membrane of the digestive tube
and has also been found in discharges from the intestines.

There are other difficulties which must be met with before
we can accept as a proved fact that infantile paralysis is a
contagious disease. Careful and masterly epidemiological
investigations of poliomyelitis have been conducted by the
Massachusetts State Board of Health extending over a
period of five years. The results of these studies were
summarized by Dr. Mark W. Richardson who plainly
brought out the fact that the disease, as observed in Massa-
chusetts, does not have the earmarks of a contagious disease.
The disease prevails in rural rather than under urban con-
ditions. In fact it shows little tendency to invade cities, and
when it does enter the city it does not strike the crowded,
congested portions of the city. In all other contagious diseases
spread through the secretions from the mouth and nose,
epidemic outbreaks have been observed in crowded sections
of cities, in asylums, hospitals, jails, on shipboard, and
similar places where the spread of infection by contact is
favored. This is the case with scarlet fever, diphtheria,
measles, mumps, whooping cough, influenza, common colds,
pneumonia, and finally cerebrospinal meningitis. Cases of
infantile paralysis in all stages of the disease have been
taken into the hospitals, orphan asylums, children's homes,
reformatory schools, and other institutions in the Common-
wealth, but in no instance during the five years in which
the disease has been studied has it ever spread under these
circumstances.

The seasonal prevalence, furthermore, of infantile paral-
ysis does not suggest the seasonal prevalence of the diseases

spread by contact through secretions from the mouth and nose. Almost all the diseases, including cerebrospinal meningitis, occur more particularly during the cold months of the year, whereas the prevalence of infantile paralysis is more marked during the summer months.

The curve of seasonal prevalence of infantile paralysis corresponds more closely with that of typhoid fever and the diarrheal diseases than it does with the group of infections spread through the secretions from the mouth and nose. Typhoid fever has its season of maximum prevalence during the warm weather. Water-borne epidemics are apt to occur in the colder months of the year, and milk outbreaks may take place at any time. Normal or residual typhoid fever is a warm weather disease and corresponds in this regard with cholera, dysentery, and the infantile diarrheas, and other intestinal infections. The only other group of diseases which prevail especially during the warm weather are those which are insect-borne. Yellow fever stops with the first frost. The most pernicious form of malaria (æstivo-autumnal) extends into the autumn, but the autumn of tropical regions is warm, rainy, and favorable to mosquito life. The season of maximum prevalence of the insect-borne diseases corresponds, of course, to the season of maximum prevalence of insect life, viz., the summer time.

It has long been evident to the student of epidemiology that the group of "contagious" diseases spread through the secretions from the mouth and nose occur throughout the entire year, but prevail especially during the colder months. On the other hand, there are two groups of diseases having their maximum seasonal prevalence during the warm weather, viz., the intestinal infections and the insect-borne diseases. Of these two groups of summer diseases the insect-borne group disappears almost to the vanishing point in temperate latitudes with wintry climates, whereas the intestinal diseases

continue to smoulder all winter long, with occasional exacer-
bations, and sometimes even with outbreaks of epidemic
proportions.   These are generalizations and may not be
applicable to a specific case.   When we study the seasonal
prevalence of infantile paralysis in all parts of the world,
however, we find a summer prevalence sometimes extending
into the fall, but dying down almost out of sight during
the winter and spring.   So far as we may judge, then, from
the seasonal prevalence of this infection, it corresponds more
closely with that of the insect-borne type than any other
group of diseases.

If poliomyelitis is a contagious disease, then we must
construct secondary theories to fit certain known facts in
its distribution, seasonal prevalence and age predilection:
facts which are at variance with this theory.   The bulk of
the cases of poliomyelitis may be very mild, and only those
cases perhaps are recognized that reach the threshold of
clinical observation.   A similar situation would be presented
if we knew diphtheria only by the cases of post-diphtheritic
paralysis.   Each case of poliomyelitis, in accordance with
the assumption that it is spread by contacts would be sur-
rounded by a number of healthy carriers, but serious epi-
demics do not occur because the infected persons are not
very susceptible.   Why epidemic outbreaks should occur in
rural conditions and not in the congested parts of cities is,
however, not explained by this assumption.   The assumed
barrier of resisting individuals apparently isolates the case,
but, in fact, favors the spread of the infection.   It seems to
be a general rule that a region where the disease had been
epidemic is spared further outbreaks later.   This phenome-
non may be explained by assuming that a large part of the
population has become immunized by having had the dis-
ease in an attenuated and unrecognized form.   It is further
assumed that in rural districts there is not the same oppor-
tunity perhaps to acquire immunity, and when an epidemic

occurs it is liable to run an exceptionally severe course. The loopholes in these conceptions are evident to students of the disease, but it is an interesting speculation that deserves careful consideration and further study.

That infantile paralysis may be an intestinal infection has not been given the consideration that it deserves. In addition to a suggestive seasonal prevalence, there is the age incidence and gastrointestinal symptoms which often usher in an attack; furthermore, we have the fact that monkeys may be infected by feeding, and the further important fact that the virus has been demonstrated in the intestinal mucosa, and even in the discharges from the bowels. No convincing outbreak of infantile paralysis has ever been associated with water, milk, meat, or other article of diet. Furthermore, we would expect a somewhat different epidemiology if food were a medium in transmitting the virus. The inherent unreliability of epidemiological data, especially of a disease such as infantile paralysis, has already been noted, and the possibility of the virus entering by the digestive tube should be borne in mind by investigators. It took a long time to learn that milk may convey scarlet fever and other infections, and that pork may be responsible for trichinosis.

There has been a suspicion that man contracts infantile paralysis from the lower animals. Hill incriminates horses. Thus, colts in Minnesota have suffered with a disease clinically like poliomyelitis, and the hypothesis has been proposed that the virus is spread through the intestinal discharges of horses which, drying, fly about as dust. A number of other students have associated it in one way or another with horses. Joest has described in detail the lesions of a disease of horses known as Bornasche's Krankheit, which has a similarity to poliomyelitis. Langhorst considers a possible relationship with the dog and cites two cases, in one of which the patient was bitten by a dog; the other

patient was licked by a dog, and at the same time had a few scratches on his hand. In both cases the diagnosis of rabies was not excluded. In fact, there are many striking resemblances between rabies and poliomyelitis. All laboratory investigators who have worked with these two diseases have been struck with this resemblance. Both diseases are acute paralytic affections. The virus in both diseases is found in its greatest concentration and virulence in the central nervous system, but is also widely diffused throughout the body. The virus of both infections is filterable, and in both affections the brunt of the lesions falls upon the neurons of the central nervous system. There are other similarities between the two diseases which should be borne in mind, especially when studying the possible relationship between poliomyelitis and dogs.

Many observations have been made in Massachusetts and elsewhere of paralytic diseases of domestic animals occurring about the same time as poliomyelitis in man. Such paralytic diseases are common among pigs and also chickens, as well as horses, dogs, cats, etc. P. Roemer reported a paralytic disease in guinea-pigs which occurred among animals in his laboratory. The guinea-pigs died of a paralysis which has some resemblance to infantile paralysis. The infection is transmissible from guinea-pig to guinea-pig by inoculation; the virus is found to be non-bacterial and filterable; the incubation period is from 9 to 12 days; the symptoms are flaccid paralysis, usually of the hind legs, with involvement of the bladder. Microscopically there is also a resemblance in the lesions of these guinea-pigs and those of poliomyelitis in man and monkeys. Roemer, however, does not claim, and there is nothing to indicate, that this paralytic disease of guinea-pigs is identical with poliomyelitis. Neustaedter has recently noted a paralytic affection of guinea-pigs that were kept in a cage under some monkeys with experimental poliomyelitis.

The evidence that any of these paralytic diseases were genuine instances of true infantile paralysis is far from convincing.

Animals suffer with many paralytic diseases, the etiology of a few of which is known, but of most of which is a pathological puzzle. The mere fact that an animal has an acute paralytic infection, with perhaps suggestive lesions in the cord, is not sufficient basis for concluding that we are dealing with poliomyelitis. All attempts to transmit the virus of infantile paralysis to all lower animals, except the monkey, have failed. Theobald Smith, Flexner and others have made numerous attempts to carry on the paralytic diseases of pigs, chickens, and other animals without success. Therefore, while it is fairly possible that some of the lower animals may suffer with poliomyelitis, perhaps in a clinically unrecognized form, and while it is possible that man may contract the infection from lower animals, the possibility is only an assumption and lacks evidence.

Another theory to account for the spread of infantile paralysis is that it is dust-borne. Hill's observations of dust and its relation to the disease in Minnesota have already been referred to. The Massachusetts State Board of Health during the five years of its epidemiological studies also considered the possibility of dust as a medium of conveying the virus, without, however, discovering any particular relationship between dust and the disease. The most suggestive evidence comes from Neustaedter and Thro, who claim to have induced the disease in monkeys by inoculating them with the dust found in sick rooms. If the virus leaves the body in any considerable amount in the secretions from the mouth and nose, it is quite conceivable that the dust of the sick room may contain the virus, for we know under certain circumstances, it retains its viability for months. Poliomyelitis does not have the characteristics of a dust-borne disease, or even of an air-borne infection,

and this hypothesis has therefore been given scant credence.

The possibility that poliomyelitis may be a wound infection has been kept in mind in the investigations made by the Massachusetts State Board of Health. No particular relationship between wounds and the disease has been made out. The resemblance between infantile paralysis and rabies has already been discussed, and the fact is plain that monkeys may be inoculated through wounds; in fact, it is possible to cause the disease in the monkeys in the greatest possible varieties of ways.

Some of the reasons for considering poliomyelitis an insect-borne disease have been published in some detail in another publication, and need not now be recounted. The epidemiological evidence collected by Brues and Sheppard, and summarized by Richardson, pointed toward the stable fly, *Stomoxys calcitrans*. The successful experiments of Rosenau and Brues, soon corroborated by Anderson and Frost, incriminate the stable fly as a factor in the transfer of the virus. The seasonal prevalence, the rural distribution and other facts concerning the disease are explained on this theory. On the other hand, the experimental facts lack further corroboration, and, moreover, these experiments have not been repeated with monkeys, and we are not justified in doing so until further studies, which are now being made, are available. Schuberg and Kuhn have recently demonstrated that a number and variety of infections may be transmitted by means of the stable fly. In their experimental work they obtained positive results with relapsing fever, anthrax, South-west African horse sickness (Pferdesterbe) and epithelioma of fowls (Hühnepocken).

Howard and Clark conducted a series of experiments on insect transmission with the virus of poliomyelitis, at the Rockefeller Institute, with very interesting results. It was found that the domestic fly (*Musca domestica*) can carry the

virus of poliomyelitis in an active state for several days on the surface of the body, and for several hours within the gastro-intestinal tract. These experiments were made by permitting the flies to feed upon the virus, then killing the insects, grinding up their bodies, filtering, and injecting the filtrate into monkeys. Howard and Clark found that mosquitoes (*Culex pipiens, C. sollicitans*, and *C. cantator*) did not take up and maintain in a living state the virus from the spinal cords of monkeys. Negative results were also obtained with lice (*Pediculus capitis* and *P. vestamenti*). The experiments with lice were designed to stimulate natural conditions, but it was found that these insects did not take the virus of the blood of monkeys or maintain it in a living state. The bedbug (*Cimex lectularius*), however, gave positive results in that it was found in one experiment to have taken the virus with the blood from infected monkeys and maintained it in a living state within the body for a period of seven days. When we consider that the virus exists in the blood of monkeys in a very dilute state, for it requires a number of cubic centimeters of blood to infect another monkey, we are almost driven to the conclusion that the virus must have become concentrated (grown ?) in the body of the bedbug. The results of Howard and Clark may therefore assume an enlarged significance.

If infantile paralysis is transmitted in nature largely or mainly through the agency of the stable fly, this fact would render the suppression of the disease comparatively easy, whereas if the infection is spread largely from person to person through the intervention of carriers and missed cases, the difficulties of the problem will be multiplied manyfold. In the case of cerebrospinal fever it has been shown that carriers are ten times as numerous as the cases; if the conditions are analogous in infantile paralysis, the suppression of the disease will probably have to wait upon specific therapy, either of a preventive or curative nature.

The health officer impatiently asks: "Is poliomyelitis a contagious disease?"   "Is it an insect-borne disease?"   "Is it dust-borne?"   "Is it contracted from lower animals?" "Is it an alimentary infection?" or, "Is it possibly like typhoid fever, spread by several or all of these various methods of conveyance?"

In the present state of our knowledge a definite answer cannot be made to these important queries, and we must await further work before the health officer can direct his measures to combat infantile paralysis with any assurance of success.   Meanwhile the public must be given the benefit of the doubt, and the infection fought along all probable lines.

THE TREATMENT OF DIABETES MELLITUS.

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THE TREATMENT OF DIABETES MELLITUS.

THE treatment of diabetes today closely resembles that prescribed by Professor Naunyn some fifteen years ago. In going over the literature one is struck by the general tendency to revert to the Naunyn methods. On account of the introduction of the various carbohydrate cures attention was diverted for a time from the basis of treatment which Naunyn prescribed.

The principals which are at the foundation of Naunyn's treatment are two — that the tendency of the disease if neglected is to progress, and that its course can be arrested for a greater or shorter length of time if the urine of the patient is kept free from sugar. If this is done a tolerance for carbohydrates may be built up. An illustration of the progressive character of the disease is shown by Case 8 in my series, a woman who developed symptoms of diabetes at the age of sixty, and showed 5.6 per cent sugar in the urine. She became sugar-free within four days, but eleven years later, when the disease was more established, three days of strict dieting failed to remove even 2 per cent of sugar from the urine. Von Noorden gives a striking example of the loss of tolerance. One of his patients showed 45 grams of sugar upon a diet containing 130 grams carbohydrate. Without change in the diet one month later the sugar in the urine had increased to 85 grams. Examples of gain in tolerance which result when the patient is made sugar-free are easy to find. A girl of thirteen did not become sugar-free until the carbohydrates in the diet were

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reduced to 10 grams, yet eleven months later she was able to tolerate 90 grams of starch without the appearance of sugar in the urine.

Various methods were recommended by Naunyn in order to render the patient sugar-free. The simplest of these consisted in merely a reduction of the total quantity of food. Many of you I am sure have seen fat diabetics whose urine would become sugar-free when the total quantity of the diet was limited sufficiently to prevent gain in weight or to produce a slight loss.

Most cases of diabetes are of mild character, in fact one is tempted to state that nearly all cases of diabetes are mild at the onset of the disease. I have shown that 25 per cent of my own cases live ten years or more. In such individuals a moderate restriction of carbohydrates suffices to render the urine sugar-free, and a tolerance for an increased quantity of carbohydrates can almost always be acquired.

The severer cases of diabetes usually become sugar-free if a very low quantity of carbohydrate is prescribed for a long time. Such an amount of carbohydrates may be 30 grams. It is surprising how often persistence in such a restricted diet leads to satisfactory results. Over and over again I have discovered that patients have become sugar-free when at the start I never expected that such a state would be reached. Coincidently with the reduction of carbohydrate should go an increase in the fat of the diet.

It is very rare that other measures are required in the ordinary types which come for treatment. But if the patient has faithfully lived upon a restricted diet for several weeks, and yet sugar remains in the urine, several procedures may be employed. The simplest expedient is to give the patient a diet without any protein, and with the carbohydrate at a minimum, in other words, what is often called a Vegetable Day. As a rule this results in a marked diminution or disappearance of the sugar. The secret of

the good of a Vegetable Day is not the vegetables, but the
absence of protein as well as of carbohydrate.   The lower-
ing of protein was considered of great advantage by Naunyn,
and its ready acceptance by the profession was made easy
through von Noorden's excellent plan of allowing vegetables
and fat to avoid a day of actual starvation.   If the Vegetable
Day fails the Starvation Day may succeed.   Naunyn
strongly favored it, and called attention to the fact that
with the patient resting in bed for the 24 hours, it was not a
hardship, and that within the subsequent one or two days the
former weight was usually regained.   I have noted with
interest that Professor von Noorden has recently pointed out
the advantages of the Starvation Day.   I can testify that
it works well, and that the urine upon it becomes sugar-
free when other measures have failed.

Such are the standard measures which in my opinion lead
to the best results in the treatment of diabetes.   I am con-
vinced of their efficacy.   It is true that occasionally a
patient or a doctor refers to cases which have apparently
done well without following the rules laid down above.
Upon investigation I think it will invariably be found that
such cases were mild or that the individuals were unusually
intelligent, and that their diet actually was a diet contain-
ing a low quantity of carbohydrate and an excess of fat with
little meat.

Diabetes is a chronic disease, and in any chronic dis-
ease one must have clearly in mind definite principles of
treatment, and confidence in them, or else in the course of
weeks, months or years one will be tempted to work a little
along this line of treatment and a little along that and in
the end no definite conclusions will be attained.

Persistence in the treatment of diabetes is essential.   I
have no hesitation in saying that the great majority of
diabetic cases which do poorly can be explained by neglect
on the part of the patient or physician in carrying out treat-

ment.   The treatment of diabetes does not demand un-
usual skill, but faithfulness is a *sine qua non*.

The simplicity of the treatment of diabetes deserves
emphasis.   It is common to hear physicians say that the
diet is too complicated and that they know little about it.
This is a great mistake, and physicians and patients suffer
equally thereby.   Most of the trouble arises because the
physician does not have his records in accessible form.   Few
data are required, in fact the essential data are simply the
total quantity of carbohydrate in the diet, and the total
quantity of sugar in the urine, but it is essential that these
data be in such a form that progress of the case can be
watched from visit to visit.   One can learn in fifteen minutes
to calculate the carbohydrate in the diabetic diet and the
fermentation test for sugar is accurate and easily per-
formed.   One must know whether the patient assimilates a
portion of the carbohydrate in the diet, that is shows a
positive carbohydrate balance, or whether the patient ex-
cretes more sugar in the urine than was contained in the
carbohydrates given, that is shows a negative carbohydrate
balance;   in other words whether the patient excretes not
only all the sugar and starch he has eaten, but also a por-
tion of the carbohydrate which has been formed out of
protein.   To render advice about treatment easy I make
use of diabetic charts by which I can see at a glance the
progress of the case.

Oatmeal is the most satisfactory of the carbohydrates
which one can give to a diabetic patient.   This is partly
due to its physical form, thus a tablespoonful of cooked oat-
meal contains only 6 grams of carbohydrate, yet with it one
can give a large quantity of cream, or if desired of butter,
and thus supply the patient with fat in a most agreeable
form.   Far more fat can be easily introduced into the diet
by the use of oatmeal than in almost any other way.   Fur-
thermore one or two tablespoonfuls of oatmeal at break-

fast solves the diabetic breakfast problem, because the balance of the meal can easily be made up of coffee, bacon and eggs. It is a great advantage for a diabetic patient to have a meal concerning which there need be no thought. His attention is sufficiently directed toward planning the diet by the remaining meals.

The mystery about von Noorden's oatmeal cure in the treatment of diabetes is still unsolved. Attempts have been made to explain it; first, by some specific body in the oatmeal which might act upon the liver or the general sugar metabolism; second, by the effect of the oatmeal upon the kidneys in rendering them less pervious to carbohydrate and it is true that there is more to be said in favor of this explanation than of the former. Although the kidneys are apparently less pervious to carbohydrate when oatmeal is given in large quantities, this does not explain why the oatmeal is oxidized or why the oatmeal cure occasionally fails. The third explanation, that of Klotz and Rosenfeld that the carbohydrate of oatmeal is so quickly fermented in the intestine that it is not absorbed as sugar but rather as decomposition products of sugar, is an attractive theory, but this is not yet upon a satisfactory basis. But this fact is true about the peculiar working of the oatmeal diet. The oatmeal diet contains a very small quantity of protein, and all the recent work has tended to confirm the early ideas of Cantani and Naunyn that an excess of protein is disadvantageous to the diabetic patient. As proof of this I would cite the work of Klemperer, who showed that one of his patients, living upon a diet containing 10 grams of protein, could take 150 grams of grape-sugar and yet excrete only 31 grams of sugar in the urine. When the quantity of protein was raised to 60 grams, the quantity of sugar in the urine rose to 37 grams, and as soon as the protein was raised to 110 grams daily, the quantity of sugar in the urine rose to 56 grams. That the protein is of vegetable

rather than of animal origin is also of significance. Another explanation lies in the fact that both before and following the oatmeal period the patient is upon a Vegetable Day, a day in which he is not only on a diet without protein, but without carbohydrate as well and still further is in a state of undernutrition. As has been said above, starvation tends to rid the organism of excess of sugar and apparently favors the oxidation of the excess of sugar there is in the body. It is thus easy to see that any carbohydrate would be better tolerated following a period of starvation than at any other time. Undoubtedly there is more of a riddle in the oatmeal day than the above explanations suggest. In the work at the Nutrition Laboratory of the Carnegie Institution the question has forced itself upon me — is the carbohydrate of the oatmeal actually oxidized? This can only be definitely proven by experiments with the respiratory apparatus. From examinations of the urine upon oatmeal days it would appear that the oatmeal is oxidized, but from respiratory experiments conducted by Dr. Benedict and myself, we have rarely, if ever, been able to show this by a rise in the respiratory quotient.

Oatmeal days are occasionally advantageous in the treatment of severe diabetes, and though it is true that other forms of carbohydrate act somewhat similarly, I believe that if one wishes to try carbohydrate days at all, it is better to use oatmeal. As you are aware, von Noorden showed that if a patient had two or three Vegetable Days he could then take large quantities of oatmeal, 250 grams, together with an equal quantity of butter for two or three days, and yet in the favorable cases the carbohydrate of the oatmeal would apparently be retained in the body and burned. Following the oatmeal period two or three Vegetable Days were prescribed. All of us have seen the advantage of such days. But we now know that it is not necessary to give so much oatmeal, and indeed, in the severer

cases is often desirable to give less.   It has also been shown that protein can be given with the oatmeal in the form of vegetable albumen without harm to the patient, and that in some cases egg albumen would be tolerated.   All agree, however, that animal albumen — meat — must be excluded.

The effects of the oatmeal are sometimes magical. Whereas the patient has had large quantities of sugar in the urine, and under systematic diet has not become sugar-free, with the oatmeal cure of two Vegetable Days, two Oatmeal Days and two Vegetable Days the urine becomes free from sugar.   On the other hand not infrequently this happy result fails to occur.   It is true that a repetition of an oatmeal period after an interval of a week or more may bring the good result desired, but occasionally it does not. The disadvantage of an oatmeal day in my opinion lies not so much in the possible indigestion which may result or in the dislike which the patient may acquire for oatmeal and butter, but rather in the fact that the patient is taken off of his beaten path of treatment, and is allowed a large quantity of carbohydrate which he has been told is harmful. He often fails to see why, if a large quantity of carbohydrate at one time can be taken with impunity, it will do harm at another.   His faith in the strict diabetic diet is unsettled. Furthermore I am doubtful of the desirability of using the oatmeal cure except rarely, because it necessitates very close observation of the patient and his attention is too much turned in upon himself.   This is contrary to my idea of the treatment of diabetes.   My aim is to place the patient upon a diet upon which he can live without loss of weight or strength, attend to his daily occupation, restricted though it may be, and yet not be confined to a hospital, or depend upon frequent visits to his physician.   I believe thoroughly in the use of occasional oatmeal days in the very severe cases of diabetes, but I am always glad to get along without them.

A word about hospital treatment. Hospital treatment is most advantageous in the treatment of diabetes, provided the cases are either moderate or severe in type. The patients learn the diet quickly, they are reassured by the gain in weight which usually results, and are given time to accommodate themselves to their new règime. On the other hand treatment for over two weeks in a hospital is seldom necessary. We all expect our patients to live five, ten or more years. They do not wish to pass this time in an institution. It is for the physician to train his patients to live upon their diet in their homes.

Acid poisoning always frightens the doctor and often needlessly. It is a pretty safe statement that if the urine is sugar-free or if the sugar in the urine is less than that of the diet, one need not worry about acid poisoning, and it is also an equally safe statement that the appearance of the patient is as good an index of the presence of acid poisoning as the reaction of the urine. I always ask the nurses of my patients to bear in mind the possibility of acid poisoning. Experienced nurses invariably warn me of its development. They are requested to instantly report anything unusual in the patient, such as loss of appetite, nausea, vomiting, listlessness, excitement, restlessness, unusual fatigue, vertigo, headache, drowsiness or discomfort. One who has seen many cases of diabetic coma learns to detect its onset by changes in the respiration. An irregular, slow, deep or painful breathing at once attracts a physician's attention, but these changes in the respiration though they occur very early, are too subtle to impress themselves upon most nurses. Of course these indications of the onset of acidosis though satisfactory are not sufficient for the careful doctor. He should determine whether the urine shows a Burgundy red color with an aqueous solution of ferric chloride, Gerhardt's test. When it does, provided the patient is not taking preparations of salicylic acid, the first

step to be taken is to keep the patient under observation
until one determines that no sudden change in his con-
dition is taking place. A telephone conversation with the
patient often relieves the doctor. In the second place it is
always safe to give from three to four teaspoonfuls of sodium
bicarbonate or sodium citrate daily, or more until the urine
is alkaline. In the third place it is most important that the
diabetic règime be not relaxed and the fight for a tolerance
of carbohydrate be abandoned, unless the patient's physical
condition compels it.

Severe acid poisoning, or for the purpose of treatment
diabetic coma, appears when the body ceases to have car-
bohydrates to burn or is unable to burn them. In all of us
there are approximately 400 grams of carbohydrate, dis-
tributed between the glycogen in the liver and that of the
muscles. If we starve or live upon a diet without carbohy-
drates, this is soon reduced and all of us will develop acid
poisoning which can be accentuated to a degree nearly
equal to that of the severest diabetic, if we simultaneously
take a great quantity of fat. The diabetic has less glycogen
in the body, consequently when he is subjected to starva-
tion he develops acid poisoning much more readily than a
healthy individual. It is important to bear in mind that
carbohydrate starvation in a diabetic may result from his
inability to take any food, such as a gastro-intestinal upset
due to an improper diet, due to seasickness, or due to lack of
food as the result of surgical operations or to unusual ex-
ertion which has consumed the little carbohydrate which his
organism contains. Forewarned, forearmed! Prevent star-
vation and one may usually prevent coma. Of course in
the severest cases of diabetes, we cannot prevent starvation,
for though we feed the patient large quantities of food, he
fails to assimilate it, and so oxidation of carbohydrate does
not occur.

As soon as the presence of severe acid poisoning appears,

watch the patient carefully from day to day. If in doubt, increase the alkali to 30 grams, but seldom to more for disturbance of digestion may result. Should the patient exhibit any premonitory signs of coma, the diet may be best relaxed by the addition of oatmeal, or if haste is needed, by giving milk with a teaspoon. Temporarily the alkali may be increased to large quantities, even a teaspoonful every hour for two or three hours, and then every hour and a half and then every two hours, not more frequently because the stomach may be upset. Not only an extra quantity of carbohydrate and alkali should be given, but pains should be taken to furnish adequate liquid with which the body can excrete the excess of acid. To prevent dilatation of the stomach it is well to give part of the liquid in the form of salt solution by the rectum. A patient with beginning coma must usually secrete at least 5 quarts of urine daily in order to come out of the same. Such a large secretion of liquid is necessary because the B-oxybutyric acid can only be removed from the body in dilute solution. Unless water is given freely the patient draws upon the fluid in the tissues to an alarming extent. The fall in weight in such cases is extremely rapid.

The treatment of actual coma is unsatisfactory. First of all one must furnish adequate fluid for the patient, second alkali is advisable. Now that we are so accustomed to the intravenous technique we may have rather better results from the introduction of a 3 per cent solution of sodium bicarbonate or even sodium carbonate, but even the best men advocate the administration of only comparatively small amounts in this way, for example 30 grams. If given promptly it will often be efficacious. Treatment of diabetic coma is its prophylaxis, and I consider it an error in treatment to allow a patient to go into coma unless the patient has been kept out of the same by the use of diet and alkalies for many months.

Surgery in diabetes is a most interesting problem. To-day it is not generally felt that the sugar *per se* is especially dangerous. Danger, however, does arise from the possibility of the patient going into coma. This occurs often as a result of carbohydrate starvation following the operation. My rule is that the patient shall be operated upon as soon as the surgeon thinks safe after a meal and that the patient shall be supplied with food as soon as possible after the operation. It is conservative for a few days preceding an operation to give alkalies in moderate doses, for example 20 grams sodium bicarbonate. If an emergency does not exist, by all means get the patient into the best possible condition by rendering him sugar-free before the operation. If the patient, however, is a severe case, I would suggest the following procedure. In a preliminary period test his ability to live upon a Vegetable and Oatmeal Day and its effect upon his metabolism. If the result is satisfactory, a week later, upon the two days preceding operation, give the patient a Vegetable Day, and immediately preceding the operation an Oatmeal Day. Sufficient carbohydrate will thus accumulate in the body to tide him over the 24 to 48 hours after the operation when eating is difficult. I have recently had a patient, who had been in diabetic coma and had recovered from the same, go through a laparotomy successfully under such a plan of treatment.

DIRECTIONS FOR NURSES IN CHARGE OF
DIABETIC PATIENTS.

1. *Collection of Urine.* Collect all urine and preserve in a bottle large enough to hold the 24-hour quantity. The urine should be voided at 7 o'clock each morning, and the 24-hour quantity measured at that time. Save at least 120 c.c. (4 oz.) as a specimen. Record date and quantity on the specimen bottle and upon the chart the quantity in cubic centimeters (c.c.) *e.g.* — November 16–17, 1620 c.c. —

1 ounce may be considered 30 c.c. (actually 29.5 c.c.).
Caution patients to save the urine while at stool.   Preserve
the urine during collection in a cool place.

2. *Weight.*   Weigh patient daily at 7 A.M. after the urine
has been voided, and note weight of clothes which should
always be the same.   Record total weight and weight of
clothes.

3. *Diet.*   (a) Record all food eaten and also record any
carbohydrate food which is served and yet not eaten.

(b) Record quantity of all food taken except that in-
cluded under Strict Diet and vegetables in the 5 per cent,
6 per cent and 10 per cent groups.

(c) The quantity of cream allowed should be measured
out before breakfast and kept in one receptacle until used.

(d) One-half ounce of butter should be served with each
meal, and the patient encouraged to take it all.   All vege-
tables should be served containing much butter, though the
butter should be made as little obvious as possible.

(e) One tablespoonful of olive oil should be used daily,
either on a salad or taken straight.

(f) The water in which vegetables are cooked should be
changed one or more times during cooking to remove car-
bohydrates.   Vegetables should be served in large portions
rather than in small portions of many vegetables.

(g) Meals are generally arranged best as follows:

Breakfast.   Coffee, cream, bacon and eggs make a stand-
ard breakfast.   If fruit is allowed a portion of the 24-hour
quantity can be taken then.   If no fruit, a single vegetable.

Dinner.   Clear soup, meat or fish, selecting a portion rich
in fat, vegetables (large portions), salad, cheese.

Supper.   Tea or cracked cocoa, one vegetable, salad.
Meat or fish, such as a thin slice of cold ham or cold corned
beef or sardines, but never serve cold meat without some
hot food.

Supper is the hardest meal to arrange, consequently a

considerable portion of the carbohydrate allowed should be saved up for that meal, whether in the form of oatmeal, bread, potato or fruit.

(*h*) Substitutes for bread, such as Akoll biscuits, Alpha biscuits and Barker's Gluten flour (Herman Barker, 433 Broadway, Somerville) can be taken while the patient is upon a strict diet, and should always be served when the diet contains only 50 grams carbohydrate.

(*i*) The quantity of carbohydrate in the diet usually prescribed can be calculated from the diet chart, but the amount of carbohydrate in the foods most commonly used is as follows:

Food.		*Weight of carbohydrate, grams*
Cream — ½ pint................	240 c.c	6
Oatmeal — one gill, dry.........	36 g.	24
One small orange or grapefruit...		10
One small apple................		15
Potatoes — two ounces..........	60 g.	12
Bread — one ounce.............	30 g.	18
Vegetables from 5 per cent, 6 per cent and 10 per cent groups eaten during 24 hours contain approximately...............		10

4. *Bowels.* The bowels should move daily using an enema if necessary. No cathartics should be given unless prescribed for the particular case.

5. *Exercise.* Exercise should be moderate. Caution patients not to get over-tired.

6. *Diversion.* Diversion should be furnished for patients, for instance, reading or games.

7. *Diabetic Coma.* Diabetic coma should always be kept in mind. Therefore, instantly report loss of appetite, nausea, vomiting, restlessness, excitement, unusual fatigue,

vertigo, headache, drowsiness, listlessness, discomfort, pain-
ful, irregular or deep breathing, because such symptoms
often precede its appearance.

8. *Vegetable Day.* Vegetables in 5 per cent and 6 per
cent groups are allowed as well as coffee, tea, cracked cocoa,
clear soups and broths, bacon. Much pains should be taken
to introduce much butter into the vegetables.

Breakfast. Coffee and two teaspoonfuls of cream, bacon,
string beans, radishes.

Lunch. Whiskey or brandy one-half ounce or sugar-free
wine 3 oz. (not always desirable), 1 Akoll biscuit or 1 cake
made from Barker's Gluten flour.

Noon Meal. Chicken broth, cabbage, lettuce, olives,
cracked cocoa (cocoa nibs).

Lunch. Same as first lunch.

Evening meal. Bouillon, bacon, spinach, celery, tea and
two teaspoonfuls of cream.

Lunch. Same as first lunch.

9. *Oatmeal Day.* Four to eight ounces of oatmeal should
be cooked for three hours with from three to six pints of
water and from one and one-half to three teaspoonfuls of salt.
Divide into from four to eight portions, and serve every two to
three hours. To each portion shortly before serving add one
ounce of butter, and cook it into that portion, being careful
not to overheat. Use only one-half ounce of butter if the
oatmeal is to be served as gruel. Care should be taken to
serve the oatmeal in an appetizing form, as the butter
easily rises to the top. Coffee, cracked cocoa, tea and
bacon are also allowed, but nothing else unless prescribed.

If the oatmeal cure is thoroughly carried out it is pre-
ceded by three days of strict diet, including vegetables in
5 per cent, 6 per cent and 10 per cent groups, and by two
Vegetable Days, and followed by the same in reverse order.

Strict Diet. Meat, poultry, game, fish, clear soups,
gelatine, eggs, butter, olive oil, coffee and tea, — and for

variety, tongue, sweetbreads, tripe, kidneys, pig's feet, brains, bone marrow, anchovies, caviar, lobster, crabs, sardines, shrimps, bologna sausage, smoked or pickled meat, or fish.

Per cent of Carbohydrates in

5 per cent or less		10 per cent ±	15 per cent ±	20 per cent ±
Lettuce	Cauliflower	Onions	Green peas	Potatoes
Spinach	Tomatoes	Squash	Artichokes	Shell beans
Sauerkraut	Rhubarb	Turnip	Parsnips	Baked beans
String beans	Egg plant	Carrots	Canned lima beans	Green corn
Celery	Leeks	Okra	Apples	Boiled rice
Asparagus	Beet greens	Beets	Pears	Boiled macaroni
Cucumbers	Watercress	Mushrooms	Apricots	
Brussels sprouts			Cherries	Plums
Sorrelo	Butternuts	Lemons	Currants	Bananas
Endive		Oranges	Raspberries	
Unsweetened and unspiced pickle		Cranberries	Huckleberries	Almonds
Ripe olives	Clams	Strawberries		
Grape fruit	Scallops	Blackberries	Pecans	
	Fish roe	Gooseberries	Filberts	
		Peaches	Walnuts	
6 per cent or Less		Pineapple	Pistachios	
Cabbage	Oysters	Watermelon	Beechnuts	
Radishes	Liver	Musk Melon		
Pumpkin				
Kohl-rabi		Brazil nuts		

Food	Protein	Fat	Carbo-hydrates	Calories
100 grams				Approximate
Beef, mutton, fowl, fish (uncooked)....	20	5–10		125–170
Ham................................	20	25		300
Bacon...............................	12	50		500
1 egg — about 50 grams, without shell .	6.5	5		75
Milk................................	3	24	5	70
Cream, good.........................	3	30	3	200
Cream, very thick....................	3	40	3	400
Butter..............................	1	85		800
Cheese..............................	25	33	2	400
Bread...............................	9	1	60	275
Wheat flour.........................	12		75	350
Rice................................	8		80	350
Oatmeal............................	16	7	66	375
Potato..............................	2		20	90

Vegetables lose carbohydrates in the cooking, especially if the water is changed twice. It is approximately correct to consider a mixture of those in the 5 per cent to 6 per cent groups as containing 3 per cent carbohydrates or 1 gram to the ounce. Meat loses 25 per cent water in the cooking.

Starch is better assimilated than sugar in glycosuric patients.

Potatoes and eggs of similar size weigh about the same.

One egg and 25 g. cooked (1 oz. uncooked) meat contain equal amounts of albumen, or approximately 1 g. nitrogen.   6.25 g. albumen contain 1 g. nitrogen.

One gill (3 tablespoonfuls) oatmeal weighs 36 g. (containing 1 g. nitrogen and 24 g. carbohydrate) and this if cooked amounts to (4 tablespoonfuls) 250 g.

Approximately 80 g. glucose may be formed from 100 g. albumen.

One gram albumen contains 4 calories.

One gram carbohydrate contains 4 calories.

One gram fat contains 9 calories.

One gram alcohol contains 7 calories.

One kilogram = 2.2 pounds. Thirty grams (g.) or cubic centimeters (c.c.) = 1 ounce.

A patient "at rest" requires 30 calories per kilogram body weight per day.

Consult the Chemical Composition of American Food Materials, Bulletin No. 28, furnished upon request to U. S. Dept. Agriculture, Office of Experiment Stations, Washington.

THE COMPLEMENT FIXATION TEST IN DIAGNOSIS.

By JAMES HOMER WRIGHT, M. D.,
of BOSTON.

THE COMPLEMENT FIXATION TEST
IN DIAGNOSIS.

THE complement fixation test, or reaction, depends upon the principle that when fresh blood serum or complement is allowed to react with a mixture of serum from an infected man or animal and an extract of the invading bacterium, it, the complement, loses or undergoes a weakening of its power to dissolve or hemolize sensitized red blood corpuscles. This was first demonstrated by Paul Bordet. The bacterial extract or antigen must be from the same species or from species closely related to the species of bacterium which infects the man or animal, and the reaction is generally regarded as specific. By means of this reaction it is possible to determine with considerable accuracy whether or not a specimen of blood serum comes from a man or animal infected with a given bacterium. This has been demonstrated for a considerable number of pathogenic bacteria and bacterial infectious diseases. Wassermann and his pupils applied the test to the diagnosis of syphilis, using as the nearest approximate to an extract of the microörganism to syphilis an extract of a congenital syphilitic liver as the antigen. It was soon shown, however, and now seems generally admitted that an extract of syphilitic liver is not essential, but that extracts from various known syphilitic organs could act as antigen in the test for syphilis. Thus the antigen in the complement fixation test for syphilis is of an entirely different character from the bacterial antigens, but notwithstanding this, it seems to be quite as specific in its action. The test has also been used with success in the diagnosis of echinococcus infection, using as antigen an extract of the parasite.

Although the complement fixation test theoretically is adaptable to a wide application in the diagnosis of infections with various bacteria, it has proven of practical value only in the last mentioned disease and in infections with the glanders bacillus, with the gonococcus and the treponema pallidum. This is due in part to the great technical difficulties of carrying out the test, and in part to the fact that easier methods of diagnosis in other bacterial infectious diseases are available. In the diagnosis of glanders it has proved of great value. I have had no experience with the test in this disease, however.

The fixation test in gonococcus infections has been extensively developed and utilized by McNeil and Schwartz. In the Pathological Laboratory of the Massachusetts General Hospital nearly 1000 tests have been performed. In this work I have been assisted by Dr. H. C. Marble. Our conclusions from these tests may be summed up as follows: A strongly positive reaction means an active infection with the gonococcus. Such reactions are usually found in gonorrheal prostatitis, active salpingitis and gonorrheal rheumatism. Weak positive reactions are common in chronic prostatitis and chronic inactive urethritis. Weak positive reactions may frequently occur in individuals who are clinically cured. They may persist for several months or more. Whether they eventually disappear in all cases after cures are effected, I have not yet determined. Certainly many individuals who are apparently cured give negative reactions. As far as our present knowledge goes, I do not think an individual should be regarded as infection free as long as he shows a weak positive reaction. With gonorrheal vaginitis and allied forms of gonococcus infections our experience has not been very extensive, but so far as it goes, it is in agreement with our experience in the cases of urethritis and prostatitis in the male.

Our results with the fixation test in syphilis and other diseases at the Massachusetts General Hospital may be summarized as follows:

Negative blood and negative clinically.   (Cases
    exclusive of the special groups named below.)   1451
Positive blood and positive clinically..........   261
                                                    ————
                                                     1712

Syphilitic aortitis and aneurysm:
   Blood positive...........................   35
      negative...........................   39
                                                    ——
                                                     74

Congenital syphilis:
   Blood positive...........................   9
      negative...........................   4
                                                    ——

	Pos.	Neg.
Tabes,—81 cases in all:		
Blood or spinal fluid, or both	41	39
Cases with both blood and spinal fluid:		
blood......................	11	22
spinal fluid..................	24	9

Syphilis of central nervous system including general paralysis and exclusive of tabes,—70 cases in all:

	Pos.	Neg.
Positive either in blood or spinal fluid, or both	35	35

	Pos.	Neg.
Cases with both blood and spinal fluid examined		
Blood........................	10	13

ARTICLE VI.

GONOCOCCUS VACCINES AND GLYCER-INE EXTRACTS OF THE GONOCOCCUS IN THE DIAGNOSIS OF GONORRHEAL INFECTIONS.

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DELIVERED June 11, 1913.

GONOCOCCUS VACCINES AND GLYCER-INE EXTRACTS OF THE GONOCOCCUS IN THE DIAGNOSIS OF GONORRHEAL INFECTIONS.

INTRODUCTION.

THE experiments described below were undertaken with the hope of finding a reliable method of diagnosis for gonorrhea by means of a specific reaction. The theoretical grounds for believing this to be possible have been discussed by earlier writers referred to below, and need not be detailed here. At this point it suffices merely to mention that changes have been shown to exist in the blood serum of patients suffering from various infectious diseases; that supposed anaphylactic reactions, like that to tuberculin, are believed to depend on changes in the serum; and that several investigators have found in the serum of patients suffering from gonorrheal infection, evidence of changes which they considered specific for gonorrhea ([11] and [12]).

As in tuberculosis, so in gonorrhea, three types of reaction have been observed after subcutaneous injection of vaccine: (a) the *local reaction* at the point of injection; (b) the *focal reaction* at the seat of the lesion; and (c) the *general reaction*, fever, malaise, etc.

Whereas previous attempts at diagnosis by means of subcutaneous injection of gonococcus vaccine have not yielded very satisfactory results, we thought it worth while to try the effects of a vaccine far more concentrated than any used heretofore, and to administer it intradermically instead of subcutaneously.

In another series of cases inoculations of vaccine were made by the method devised by v. Pirquet for the skin tuberculin test; and, in a third group, glycerine extracts were employed in like manner.

PART I: SERIES 1 AND 2.

METHOD, DOSAGE, MATERIAL.

The vaccine was prepared from nine strains of gonococci, which had been under artificial cultivation for varying lengths of time. The organisms were suspended in normal salt solution, standardized by count to 500 million per 0.1 c.c., and mixed with ½ per cent of lysol. The first injections were given several days after the preparation of the vaccine when it had been shown by culture to be sterile. Heat was not used to kill the bacteria as they die quickly under the above conditions. Subsequent cultures showed that the vaccines remained sterile while in use.

Normal salt solution containing ½ per cent of lysol was used as a control solution.

Before administering the vaccine or control, the skin of the back of each arm was carefully cleaned. The vaccine was introduced intradermically; i.e., beneath the superficial layer of the skin in the same way in which cocaine is used for local anæsthesia. The control solution was given similarly in the other arm.

The dose in the first, and in nearly all subsequent cases, was 500 million gonococci, or 0.1 c.c. of the vaccine. One patient, having fever, was given 300 million to begin with, but received 500 million when convalescent. Another received 150 million, and a third 100 million. There were no other exceptions.

The clinical material came partly from the out-patient department of the Massachusetts General Hospital, but chiefly from the hospital wards. Thirty-two patients were

studied, of whom fourteen showed evidence of active gonor-
rheal infection in some form; thirteen had unrelated dis-
eases; and five were healthy. "Table No. I" shows more
definitely the distribution of material.

FIRST SERIES: RESULTS.

The local reactions generally began in about six hours, were
fully developed after twenty-four hours and disappeared grad-
ually in the course of two or three days. They consisted of
redness, swelling and tenderness over a zone several centi-
meters in diameter, surrounding a central area which was
more deeply injected and sometimes elevated. Severe re-
actions showed larger zones and were somewhat painful.

The injections of the control solution left behind only the
mark of the needle puncture. Table I shows that local
reactions occurred in all the gonorrheal cases and in all but
three of the non-gonorrheal or control cases; that most of
the reactions were marked; and that the proportion of
marked reactions was nearly as great in the control as in the
gonorrheal cases.

Closer analysis shows that the first test was made on a
case of chronic prostatitis, and that a severe local reaction
developed. The three following tests were made on con-
trol cases, and they did not react at all. Their respective
diagnoses were abscess following typhoid, fistula in ano, and
carcinoma of the breast. The fifth case had acute anterior
urethritis, and gave a marked reaction. These five tests
were made within the first week after the preparation of
the vaccine, and their outcome was distinctively encourag-
ing.

All subsequent injections of vaccine, however, gave
positive local reactions; and although tests were made over
a period of 109 days after the first use of this vaccine, no
other striking change in its effect was seen.

These results led us to believe that the vaccine, which

had seemed to act specifically during the first week, had subsequently developed irritating properties of a non-specific nature. Acting on this hypothesis, we made a second series of tests with a fresh vaccine. The results are shown in Table II.

TABLE I.

LOCAL REACTIONS: FIRST SERIES.

Gonorrheal Cases: 14.

Diagnosis.	No reaction.	Slight Reaction.	Marked Reaction.	Severe Reaction.	Number of Cases
Acute urethritis................	..	..	3	..	3
Chronic urethritis or prostatitis..	..	..	3	1	4
Salpingitis....................	..	1	1	1	3
Arthritis of gonorrheal type.....	..	..	3	1	4
Control Cases: 18.					
Normal persons................	..	1	3	1	5
Various diseases...............	3	5	4	1	13
Totals of reactions.............	3	7	17	5	32

TABLE II.

LOCAL REACTIONS: SECOND SERIES.

Gonorrheal Cases: 3.

Diagnosis.	Slight Reaction.	Marked Reaction.	Number of Cases.
Acute urethritis with arthritis.	1	..	1
Chronic gonorrheal infection..	..	2	2
Control Cases: 11.			
Normal persons...............	..	2	2
Various diseases..............	4	5	9

SECOND SERIES.

All cases inoculated with the second vaccine showed reactions, although the tests were made within a week of its preparation.

The two vaccines used were prepared in the same way by the same person; both were standardized by count to 500 million per 0.1 c.c. and both were administered in the same way and in the same dose. Nevertheless, the vaccines were not identical. The first was made from several strains which had been kept for some time in the laboratory and to these were added several freshly isolated cultures. The second vaccine was made from a new set of fresh cultures. Such differences of origin might, perhaps, cause a difference of toxicity or of irritating properties in two vaccines. Irons[3] points out that the degree of reaction depends not only on the number of gonococci inoculated, but also on the source and age of the cultures from which the vaccine is prepared. He found that cultures isolated within three months furnished a vaccine ten times as strong as a culture which had been grown in the laboratory for two years.

We are inclined to believe that our vaccines possessed irritating properties of a non-specific nature, and that if there was any specific reaction, it was masked by the response to the irritant.

If the hypothesis be advanced that better results might have been obtained with smaller dosage, it may be replied that our dosage was not larger than that frequently used by Irons for diagnostic tests; and that general and focal reactions in our series were neither many nor well-marked; also, this hypothesis does not explain the three negative tests. There seems little reason to suppose that the outcome of the local reactions would have been essentially different had injections been given subcutaneously instead of intradermically.

A focal reaction was observed in only one case of the entire number, 46 in all. The reaction consisted of increase of pain in the affected joints of a patient supposed to have gonorrheal arthritis. Three other cases of arthritis, probably gonorrheal, and four salpingitis cases gave no such reaction.

Symptoms attributable to a general reaction were carefully looked for, and four hourly charts were kept for 32 ward-patients. Eight of these, including two control patients, showed slight elevations of temperature appearing some hours after the injection. One of the controls had had variations of temperature before the test, and after it his temperature rose from 97 degrees to 100.3 degrees, the greatest increase noted.

In the gonorrheal cases the temperature rise ranged from $\frac{1}{2}$ degree to 1.2 degrees. The patients who had been running slightly elevated temperatures before the test showed increase of fever. Elevations of temperature occurred in three of the four cases of arthritis, and in two of the four salpingitis cases. None of those who responded with fever complained of malaise, but one of them showed the focal reaction mentioned above.

Malaise was noted, however, in two other gonorrheal and in two control cases.

Stated briefly, the results from injection of vaccine in 46 cases show that local reactions appeared in all gonorrheal and in nearly all non-gonorrheal cases; that there were signs suggesting a general reaction in eight gonorrheal cases and in two non-gonorrhoeal cases; and that a focal reaction was observed in one case only, the diagnosis in this case being gonorrheal arthritis.

LITERATURE.

The local reaction is generally conceded to be unreliable for diagnosis. Although the most common of the

three reactions, local manifestations have been observed repeatedly when it was believed that active and preëxisting gonorrhea could be excluded. Such reactions may closely resemble those of gonorrheal cases; and, according to Guggisberg[8], indifferent subcutaneous injections may cause painful efflorescence in sensitive persons. The local reaction in gonorrhea is generally more marked and of longer duration than that which may appear in normal individuals, but these reactions have not yet been sharply differentiated.

General reactions consisting of fever, rapid pulse, headache, lassitude and leucocytosis, or of any of these symptoms, have been observed in a comparatively small number of cases. According to Guggisberg the general reaction occurs most often in fresh infections when acute inflammation has existed recently. Irons[1] says that the fever may be so slight as easily to escape notice, but Fromme and Collmann[7] think that a rise of temperature following the injection of the vaccine may perhaps help in differentiating extra-uterine pregnancy from salpingitis. This hypothesis lacks confirmation. Apparently, no general reaction has been recorded in a non-gonorrheal case.

The focal reaction merits closer analysis. Pain and swelling were observed by Irons[1] in a considerable number of cases of gonorrheal arthritis, and he attributed to these signs, plus fever, a certain value for distinguishing gonorrheal from other forms of arthritis. He says that a positive reaction can generally be obtained at will in gonorrheal arthritis by means of graduated doses. In a case of post-operative periurethral abscess without secondary infection or retention of pus he saw a "marked increase of redness and tenderness about the wound." He says, further, that ocular reactions are sometimes observed in cases in which iritis has previously been present, and that increased inflammation or effusions into the eye are not in-

frequent after therapeutic inoculations of vaccine in active gonorrheal iritis.

In women having gonorrheal salpingitis or allied diseases, increase of pain and of localized tenderness, increase of discharge, and hemorrhages or premature menstruation have been observed repeatedly. Some of these symptoms have been noted in a considerable proportion of cases of this kind by Reiter[5], Köhler[6], Fromme and Collmann[7] and by Guggisberg[8]. The latter has twice found gonococci in the discharge after injection, having failed to find them previously.

Fromme and Collmann, on the other hand, saw marked focal reactions in three cases thought not to be infected with gonorrhea and emphasized the occurrence of a focal reaction in a virgin who had a myoma. Guggisberg recorded a marked positive reaction in one case of septic infection.

Of fundamental importance to those interested in vaccine diagnosis, and in treatment as well, is the work of E. C. Rosenow[9] on autolysis of bacteria. He showed that the gonococcus and some other organisms undergo rapid autolysis in normal salt solution; that at a certain period of autolysis the mixture becomes extremely toxic; and that the time the acutely toxic substance appears in solution is directly proportional to the activity of the autolytic ferment and the rate of disintegration of the organisms. Suspensions of the gonococcus in salt solution when incubated at 37° C. became toxic to guinea-pigs after 10 minutes, more so after one hour, and were non-toxic again after 20 hours. With the staphylococcus aureus, little or no proteolysis occurred under similar conditions.

DISCUSSION.

Although irritating properties manifested by injection into human beings and toxicity in guinea-pigs are not the

same, there seems to be an analogy between the development of toxic products by autolysis in Rosenow's experiments and the appearance of irritating properties in our vaccines; moreover, it is the experience of Dr. Albert E. Steele, Assistant in Clinical Bacteriology at the Massachusetts General Hospital, that gonococcus vaccine autolyses within a few days, even when prepared with lysol and kept in an ice-chest. If autolysis of bacterial suspensions be delayed by lysol and by cold, it follows that the lysol must be added promptly to suspensions of gonococci, and the suspensions must be placed as soon as practicable in an ice-chest if the formation in them of toxic substances is to be delayed.

If the same line of reasoning be applied hypothetically to the supposed formation in gonococcus vaccine of substances irritating to human beings it becomes apparent that two vaccines similarly prepared might be different in action provided that, in the first instance, the lysol were added to the suspension immediately and the mixture placed at once in an ice-chest and, in the second instance, the lysol were added some hours later, the suspension having stood meanwhile at room temperature. Another important discovery of Rosenow is the fact that recently isolated cultures of the gonococcus autolyse more rapidly than do older cultures.[10]

Whether or not any such factors may have caused the difference in action of our two vaccines, one of which appeared to have been non-irritating during the first week, and the other irritating from the start, is a question which suggests itself to the writers, but which they are unable to answer from information at hand.

Returning to the facts that suspensions of gonococci become quickly toxic to guinea-pigs and later again non-toxic, and that this change corresponds to the rate of autolysis, it may be asked what influence this autolysis has on the

immunizing properties of a vaccine, and whether or not these properties may be destroyed by autolysis.

Some light may perhaps be thrown on the question by comparing the clinical value of gonococcus vaccine with that of staphylococcus vaccine, which Rosenow showed did not autolyse to any extent in normal salt solution. Staphylococcus vaccine has to a high degree the power of influencing favorably localized foci of staphylococcus infection; whereas, gonococcus vaccine is generally conceded to be one of the less efficacious of the vaccines similarly used.

When a vaccine has undergone autolysis to an unknown degree, when changes in it may still be taking place, and when the peculiar proteins of the original organism may perhaps have been destroyed or modified, the results of diagnostic tests and of treatment with such a vaccine may well prove unreliable; and, did a specific reaction occur, it might be masked by the effects of irritating or non-specific toxic products of disintegration of the bacteria.

These considerations indicate that more knowledge is needed of the changes which take place in gonococcus vaccine, and raise the hope that more satisfactory results may follow improved methods of preparing vaccine.

PART II: INOCULATION OF VACCINE BY THE VON PIRQUET METHOD.

While the second series of injections was being conducted in the wards, a group of out-patients was tested with the same vaccine, inoculated by the method devised by von Pirquet for the tuberculin test. Inoculations of the vaccine were always made in two places with a control scarification between them, and, in every instance, a control solution was used in like manner.

The cases, 15 in number, ranged from acute anterior urethritis to chronic posterior urethritis and prostatitis. One of the patients was seen again on the day following

the inoculation, 10 were seen on the second day, and 4 not until the third day.

There resulted, as a rule, only a minute scab at every scarification point, but occasionally there was found a slight redness a few millimeters in diameter. No swelling and no papule was observed in any of these cases on the days subsequent to the inoculation; but sometimes a small wheal formed quickly at all scarifications. In consideration of the dirtiness of many of the patients and the fact that the redness was seen nearly as often at control-scarifications as at the points of inoculation of the vaccine, slight redness was attributed to superficial infection. It is conceded that very slight or evanescent specific reactions may have been overlooked because close observation of results was impossible under the circumstances.

DISCUSSION AND SUMMARY.

The von Pirquet technic of inoculation was first used by Köhler,[6] who tested, in this way, several gonococcus vaccines. He says that during the first hour after inoculation a slight swelling appeared, and that it continued to increase for four or five hours until it reached about the size of a lentil. After from 18 to 24 hours it began to fade, and on the second day it was scarcely recognizable. The swelling was often surrounded by a red areola. Köhler observed this phenomenon in many gonorrheal cases, and likened it to the von Pirquet tuberculin reaction, but he says that it was never so definite as is a positive reaction to tuberculin. Control inoculations showed a similar slight swelling after one hour. It decreased after 4 or 5 hours, and, as a rule, it was entirely gone in from 8 to 12 hours.

Although their vaccine was, probably, much more concentrated than any used by Köhler, the writers obtained no results comparable with his. They failed to observe anything resembling a positive tuberculin test in 15 cases of

gonorrheal infection, which included all stages of the disease from the acute to the most chronic types of genito-urinary infection in the male.

PART III: GLYCERINE EXTRACTS.

PREPARATION AND TECHNIC.

Three extracts were prepared. For each of them the gonococci in 12 culture tubes of human blood agar were washed off with a small amount of distilled water, 0.5 per cent of carbolic acid added, and the mixture placed in the incubator at 37° C. "Extract I" was incubated for 24 hours, and then heated at 60° C. for 2 hours. "Extract No. II" was incubated for 48 hours, and heated at 60 degrees for 2 hours, and "Extract III" was not incubated but was heated immediately at 60 degrees for 2 hours. To each of these extracts 2 c.c. of glycerine were added after the heating, and, finally, all was evaporated in an air blast to a small volume. The resulting extracts were viscid and cloudy.

The control solution was made similarly, but from sterile culture tubes.

The extracts were kept in bottles covered with rubber nipples and they remained in an ice-chest except when taken out to withdraw material for the tests. This was done aseptically by means of a hypodermic syringe and enough of the vaccine was taken out each time to suffice for the work of the day.

Inoculations were made by the von Pirquet method; a control scarification without any inoculation was made first, and then the vaccine was inoculated on either side of it. The control solution was inoculated in the same way at two other points with a scarification between.

Cultures on blood serum and on plain agar showed the extracts to be sterile before they were used, and again after completion of the tests.

WORK AND RESULTS WITH "EXTRACT I."

Twelve of the seventeen patients in this series had gonorrhea, in three other cases its presence was suspected, and two were believed to be free from it. Seven of the patients, including four gonorrheal cases and one in which gonorrhea was suspected, were seen at 24 and 48 hours after the inoculation. The remaining ten, being out-patients, were not seen until the third day. There were among them eight cases of acute or chronic gonorrhea and two of arthritis due, presumably, to gonorrhea.

Very slight redness was noted once at a control mark and once where the gonococcus extract had been inoculated.

Nothing resembling a specific reaction was observed in this series.

WORK AND RESULTS WITH "EXTRACT II."

In the series of 15 patients 12 had gonorrhea, and in the remaining three its presence was suspected. Acute and chronic urethritis, acute exacerbations of chronic urethritis, epididymitis and salpingitis were included in the series. Seven ward-patients were revisited after 24 hours, 48 hours, and 4 days. Five out-patients were seen on the second day, and three on the third day.

Seven cases, two of them in the wards, showed no reaction at all.

Five cases, three of which were in the wards, showed slight redness at both points of inoculation of the vaccine. These reactions were considered of questionable significance.

Three cases, two of them in the wards, showed a small area of redness with central swelling at both points of vaccine inoculation. These reactions were classed as positive.

Slight redness without swelling occurred at one control mark in two patients, and at two control marks in one patient. It was attributed to infection.

The result with "Extract II" was no reaction in seven cases, a questionable reaction in five cases, and a positive reaction in three cases.

WORK AND RESULTS WITH "EXTRACT III."

There were 15 patients in the series of whom 11 had chronic urethritis or prostatitis, 2 sub-acute urethritis, and 2 arthritis, supposedly of gonorrheal origin. Six ward patients were seen daily after the inoculation as long as any reaction was visible, and of the 9 out-patients 5 were seen on the second, 3 on the third day, and one which reacted returned on the second and third days.

Six out-patients and 3 ward-patients showed no change, 2 ward cases and one out-patient case gave questionable reactions, and 3 gave positive reactions. The control marks in two cases of doubtful reaction showed slight redness. The outcome of reactions was judged by the same criteria as for "Extract II."

SUMMARY OF WORK WITH EXTRACTS I, II AND III.

The total number of tests with these extracts was 48, and the number made with each extract was about the same.

Extract I gave nothing resembling a specific reaction.

Of 30 tests with Extracts II and III 16 were negative, 8 were doubtful, and 6 gave reactions resembling those seen in positive skin-tests made with tuberculin by the von Pirquet technic. The papules, however, were decidedly smaller than those of a well-marked tuberculin test. It is worthy of note that all positive tests occurred in patients having a definitely active gonorrhea, and that the outcome of the tests in the more chronic and the latent cases was uniformly negative.

DISCUSSION: EXTRACTS.

The technic followed by Dr. Steele in preparing our extracts was outlined by Dr. E. E. Irons of Chicago in a letter

to Steele, and the latter followed the directions with the greatest care. Owing to Dr. Steele's experience in the preparation of vaccines, we believe that errors of technic can be excluded.

The extracts and also the control solution were cloudy and contained a brownish sediment due apparently to blood elements washed from the media with the bacteria. The sediments were amorphous as seen under an oil-immersion lens. They showed no sign of recognizable bacterial elements.

Iron does not state in figures the proportion of gonorrheal cases in which he observed well-marked reactions with gonococcin, but his paper leaves with us the impression that the reactions occurred in a considerable proportion of the gonorrheal cases. Fairly marked reactions were seen by him in adults occasionally, and in children more frequently when previous gonococcal infection could be ruled out; and reactions were obtained with gonococcin in epidemic meningitis and with meningococcus extracts in gonorrhea. Believing that infections with the micrococcus catarrhalis and other allied organisms might give a like response to gonococcin, Irons points out that such infections must be excluded before a positive reaction can be attributed to gonorrhea. He suggests also that the reaction may be characteristic of a group of infections rather than of a single disease, and says that a positive reaction should be regarded merely as confirmatory evidence of gonorrhea.

The comparatively small number of tests made by us does not admit of detailed deductions. We infer from them, however, that our proportion of definitely positive reactions was probably less than that of Irons and that doubtful results were relatively numerous. We are inclined to believe that the papules seen in the "positive" cases indicate a specific or a group reaction; and that redness without

papule-formation should be regarded as due, probably, to infection or to other accidental causes.

In a letter received recently from Dr. Irons, he attributes the cloudiness of our extracts to blood particles washed from the media, and advises the use of ascites agar or of blood agar in which the blood has been mixed with the agar before it hardens. He says, further, that some extracts are not nearly so satisfactory as others, and suggests that this may be due to differences in the degree of autolysis of the bacterial protein.

CONCLUSIONS.

A. FROM PUBLISHED WORK OF OTHERS REFERRED TO ABOVE:

1. Reactions thus far observed after injections of gonococcus vaccine have not been clearly specific for gonorrheal infection.

2. The reactions seem to show a selective action in some types of gonorrheal disease.

3. Local reactions after injection are common in nongonorrheal cases. They are not valuable either for the diagnosis of gonorrhea or for demonstration of its cure.

4. Focal reactions are seen frequently in active gonorrheal arthritis and salpingitis; but, whereas they have been observed in cases showing no other evidence of gonorrhoea, their diagnostic value is small.

5. A general reaction is seldom noticeable, and it may be easily simulated by slight symptoms due to other causes. It has, *per se*, no diagnostic value.

6. Gonococcus vaccine autolyses rapidly, and thus undergoes changes little known.

B. FROM WRITERS' WORK:

1. The concentrated vaccine used by the writers showed no superiority for diagnostic tests.

2. It produced in gonorrheal and in control cases a local lesion like that of a chemical irritant. We think that autolysis may have been a factor in producing the supposedly irritating properties of our vaccine; that the changes in the vaccine may have prevented it from producing a specific reaction; and that the unsatisfactory therapeutic effects of gonococcus vaccine may, perhaps, be traceable to autolysis.

4. Glycerine extracts of the gonococcus inoculated by the method of von Pirquet caused, in a few cases, the formation of peculiar papules which may have represented a specific reaction. Most of the cases showed no definite reaction.

5. Although our tests were negative in the main, and although the work of others using similar methods has yielded unsatisfactory results for diagnosis we desire to emphasize our belief that failures serve as guideposts to progress, and that present knowledge justifies the hope that a valuable diagnostic test for gonorrheal infection may yet be devised through improved methods of preparing vaccines or extracts of the gonococcus.

It is with great pleasure that we express our thanks and obligation to Dr. Albert E. Steele for preparing the vaccines and the extracts which we used, and to Dr. Hugh Cabot, as well as to many other members of the Staff of the Massachusetts General Hospital, for the opportunity to study their patients.

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THE PATHOLOGICAL LESION OF WHOOPING COUGH.

By F. B. MALLORY, M.D.,
OF BROOKLINE.

THE PATHOLOGICAL LESION OF
WHOOPING COUGH.

THE whooping cough bacillus was discovered by Bordet
and Gengou in 1900, but was not obtained by them in pure
culture until 1906. They found it in large numbers in the
sputum of all early cases of the disease examined. The
organism is a minute ovoid, Gram-negative cocco-bacillus
which stains lightly by the ordinary methods. It is about
the size of the influenza bacillus. They were able to start
cultures only on a potato-blood-agar medium which they
devised. They were also able to obtain a complement fix-
ation test by using an emulsion of the organism and serum
from a patient's blood. This test showed fairly conclusively
that the patient produced an antibody for the organism,
and that reaction has been the basis of the proof since that
date that the organism causes the disease. Still, in spite of the
fact that the bacillus has been generally accepted by bac-
teriologists as the cause of whooping cough, it has not been
accepted to any extent by the medical profession because
the organism has never been demonstrated in connection
with any lesion, only in connection with the disease.

In 1908 Klimenko repeated the work of Bordet and Gen-
gou and confirmed their results. He also inoculated a
number of monkeys and puppies with pure cultures of the
bacillus. Most of the puppies died in the course of a few
weeks. They coughed and sneezed, but never whooped.
After the animals died or were killed he was able to ob-
tain the pertussis bacillus again from them in pure culture.

Our work on whooping cough at the Boston City Hospital
started from a chance observation. In going over the sec-

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tions from an acute case of whooping cough microscopically
with one of the pathological internes, I noticed what seemed
to be minute organisms packed in large numbers between
the cilia of the epithelial cells lining the trachea.   Better
sections and stains showed the organisms to be minute
bacilli.   They were present in great numbers, dozens to a
hundred or more, over the surface of each cell.   Sections
from the trachea of another case where the disease had
lasted six weeks show similar bacilli present but only in small
numbers.

Lung tissue from three other cases was obtained and
showed similar organisms between the cilia of the cells lining
the bronchi.   The bacilli were also found free in the bronchial
secretion and enclosed in polymorphonuclear leucocytes, but
they were never found within the alveoli.   The broncho-
pneumonia which so often complicates whooping cough
seems to be due entirely to other contaminating organisms.

The action of the bacillus pertussis seems to be largely
mechanical.   It interferes with the normal movements of
the cilia and therefore furnishes a continual irritation which
excites the coughing.

The organism also secretes a mild toxin as is shown in
three ways by a slight inflammatory exudation, by a lympho-
cytosis and by the production of a specific antibody.

The finding of this peculiar lesion naturally suggested ex-
perimental work.   We first obtained sputum from acute
cases of whooping cough and inoculated it into the trachea
of a puppy and of a rabbit.   Later the animals were killed
and the respiratory tract studied microscopically.   Organ-
isms identical in every way with those found in whooping
cough were present between the cilia in the trachea and
bronchi of both animals.

Attempts were next made to obtain pure cultures and
after considerable effort we succeeded in getting three
different strains.   These were inoculated into a number of
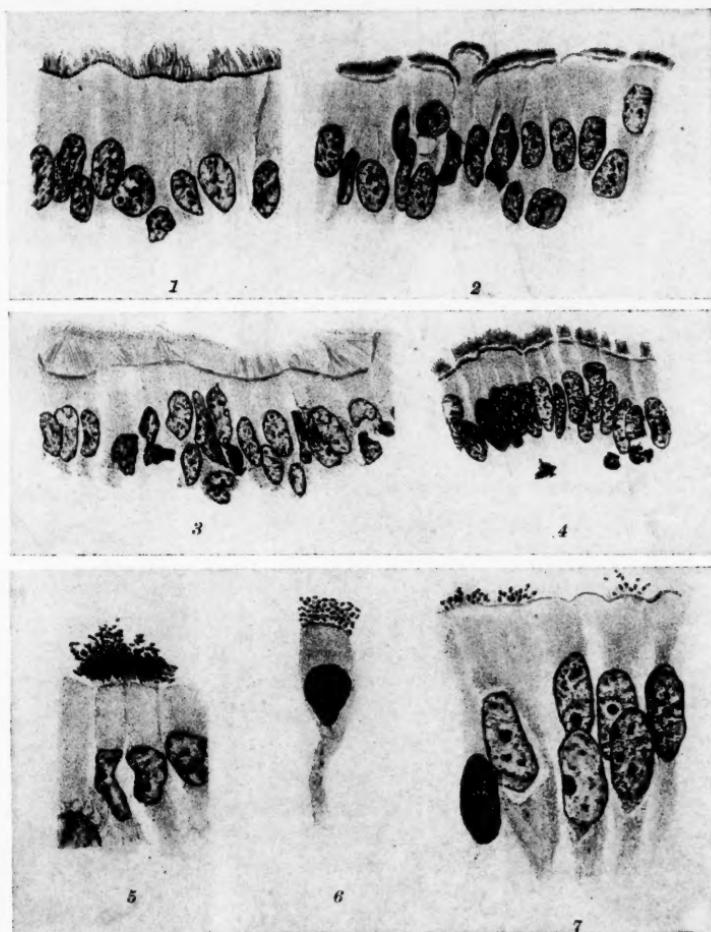
DESCRIPTION OF PLATE.

[The drawings are by Miss Etta R. Piotti. The magnifications are approximate.]

FIG. 1.—Ciliated epithelium lining normal trachea of child. x 1,000.

FIG. 2.—Ciliated epithelium lining trachea of child dying in acute stage of whooping cough. Large numbers of minute bacilli present between the cilia. x 1,000.

FIG. 3.—Ciliated epithelium lining bronchus of child; mucus forming in cells and collecting on surface. x 1,000.

FIG. 4.—Ciliated epithelium lining bronchus of child dying in acute stage of whooping cough. Masses of minute bacilli present between the cilia. x 1,000.

FIG. 5.—Minute bacilli present in masses between cilia of two cells lining trachea. x 1,500.

FIG. 6.—Desquamating epithelial cell in trachea with numerous bacilli between cilia. x 1,500.

FIG. 7.—Ciliated epithelium from trachea of child dying at a late stage of whooping cough. Bacilli still present in small numbers between cilia. x 1500.

puppies and rabbits which were killed after a varying number of days. In many of them we found bacilli often in large numbers between the cilia of the cells lining the nares, trachea and bronchi, and obtained them again, as we believed, in pure culture.

The lesions of whooping cough as found in man have been controlled by the examination of trachea and bronchi from hundreds of other diseases. No similar lesion has been found in any of them. The experimental work on animals is open to a certain amount of doubt, owing to a recent observation made by Dr. L. J. Rhea and here appended.

"While reading Dr. Mallory's first contribution on the pathology of whooping cough I was impressed with the general similarity between this disease and canine distemper, a disease common among dogs, and thought it might be worth while to study the pathology of this disease, using the technique employed by Dr. Mallory in his work on whooping cough. A number of dogs have been examined. Some of these were normal, the others had distemper. The normal dogs showed no lesions referable to distemper, but in the others a pathological lesion was found which was very similar to that found in whooping cough. This lesion consists of a rather superficial inflammatory reaction, especially in the trachea and bronchi.

Besides this inflammatory reaction there are in the cilia of the epithelial cells of the respiratory tract very many small organisms which I have been unable to distinguish morphologically from the Bordet-Gengou bacillus. These organisms are in the cilia of the epithelial cells attached to the respiratory tract and in the desquamated epithelial cells as well. The similarity in the histological lesions and the exciting organism in whooping cough and canine distemper is of some interest from the view-point of comparative pathology and I believe of real importance in

experimental work with whooping cough. If one is to use in the study of whooping cough laboratory animals that are subject to a disease produced by an organism which is found in the same anatomical situation and is so similar morphologically to the organism producing whooping cough, the interpretation of results is made with difficulty. Such work must be controlled by means other than histological. But the observations referred to above do not in any way detract from experimental work along these lines. On the contrary it suggests an interesting relationship between the two exciting organisms; the bacillus of Bordet-Gengou, the cause of whooping cough, and the bacillus bronchisepticus, the cause of canine distemper.

"I might add that an organism similar in its morphology and anatomical situation has been found in rabbits suffering with snuffles, and what has been said in regard to canine distemper can be said in regard to snuffles in rabbits.

"Besides the general medical interest in the work Dr. Mallory has just reported, this work illustrates the importance of the proper application of histological technique to problems in pathology. But it takes a Dr. Mallory to show us how to apply this technique."

In conclusion I should like to add that Dr. L. W. Gorham has recently repeated some of the experimental work, starting with a new culture of the whooping cough bacillus obtained from an acute case of the disease. He used six young rabbits from one litter. Two were inoculated daily for a week with a suspension of the whooping cough bacillus. They lost weight and died at the end of ten days. Two others were inoculated in the same way with the influenza bacillus, one with the pyocyaneus, and one with normal salt solution. These four were killed at the end of ten days. Sections of the nares, trachea and bronchi from the

two animals inoculated with the whooping cough bacillus showed great numbers of minute bacilli between the cilia. Pure cultures were obtained from one of the animals; but it was the bacillus bronchisepticus, not the bacillus pertussis. Cultures from the other rabbit were badly contaminated. Cultures and sections from the four other animals from the same litter were entirely negative so far as the bacillus bronchisepticus was concerned.

Further experimental work is evidently needed in order to clear up the subject. The two organisms closely resemble each other morphologically and in cultures on potato-blood-agar, but can be distinguished by their differences in motility and their alkali production in litmus milk.

SYMPOSIUM ON NEPHRITIS.

ARTICLES VIII TO XIV.

ARTICLE VIII.

THE CLASSIFICATION OF NEPHRITIS FROM THE PATHOLOGICAL POINT OF VIEW.

By F. B. MALLORY, M.D.,
of Brookline.

Delivered June 10, 1913.

THE CLASSIFICATION OF NEPHRITIS FROM THE PATHOLOGICAL POINT OF VIEW.

THE inflammatory lesions of the kidney are caused, for the most part, by toxins of various sorts brought to it by the circulating blood and by infectious agents, chiefly bacteria, which reach it ordinarily through the blood or through the ureter. The lesions may be divided, therefore, primarily into two groups, the toxic and the infectious. It is the first or toxic group which the clinician has in mind when he thinks of nephritis.

In studying the lesions of the kidney it is important to bear in mind that it is composed of a large number of small units. Every unit consists of an afferent vessel, of a glomerulus composed of a knot of capillaries, and of a tubule. The blind invaginated end of the tubule is applied to the surface of the glomerulus. Its actual beginning is known as the capsular space. In addition to these four main structures of a unit there is an efferent vessel and a network of capillaries derived from it and surrounding the tubule. These vessels are of minor importance. A little connective tissue surrounds the vessels and tubule and extends in small amount into the glomerulus.

Of these different structures in a unit the glomerulus, where blood vessel and epithelium are in close association, seems the most susceptible to the action of injurious agents.

If any one of the four essential parts of a renal unit is destroyed, the other three in time atrophy and cease to function. Each part is useless without the other three.

In order to understand the lesions of the kidney it is necessary to separate it into its units and study the effect of injurious agents on each part of the unit.

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The toxic lesions of the kidney are best classified on an anatomical basis, *i.e.* according to the part of the renal unit most affected. This classification gives four groups which form the type lesions; they are as follows:

1. Tubular nephritis.
2. Capsular glomerulonephritis.
. 3. Intracapillary glomerulonephritis.
4. Vascular nephritis (arteriosclerosis).

Each one of these varieties may occur practically in pure form, but the first three may be, and often are, combined in varying proportions. Whether the first three can be recognized clinically as three distinct types is doubtful. While usually acute, they also occur in subacute and chronic form; vascular nephritis is always chronic.

TUBULAR NEPHRITIS.

The term tubular nephritis is used when degeneration and necrosis of the renal epithelium occur as the result of the action of diffusible toxins excreted through the kidneys. The lesion is limited almost exclusively to the cortex and involves chiefly the cells lining the convoluted tubules. The lesion may be extensive and diffuse or occur in small scattered foci. It may exist by itself or complicate the different forms of glomerulonephritis.

Tubular nephritis may be caused by a variety of toxins and poisons, so that the resulting inflammatory reaction is not always the same. In rare instances the toxin is strong, acts quickly, and causes extensive necrosis of nearly all the epithelial cells lining the convoluted tubules. The lumina become filled with the necrotic desquamated cells which attract polymorphonuclear and endothelial leucocytes in varying numbers. Some tubules contain serum and networks of fibrin. In addition there may be some edema and

KIDNEY.

Acute tubular nephritis following abortion and streptococcus peritonitis. Tubules filled with necrotic desquamated epithelial cells. Regeneration occurring along the tubular wall outside of them.
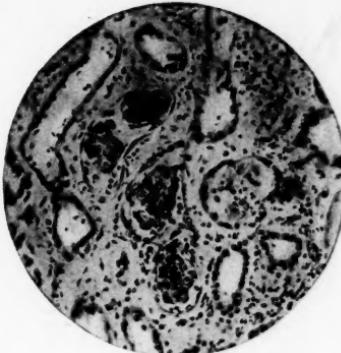

KIDNEY.

Acute tubular nephritis due to corrosive sublimate poisoning. Some of the tubules contain necrotic desquamated epithelial cells which are being surrounded and digested by endothelial leucocytes.

KIDNEY.

Acute tubular nephritis occurring in scarlet fever. The tubules contain fibrin and polymorphonuclear leucocytes. The intertubular tissue is infiltrated with numerous lymphocytes and also with some polymorphonuclear and endothelial leucocytes.
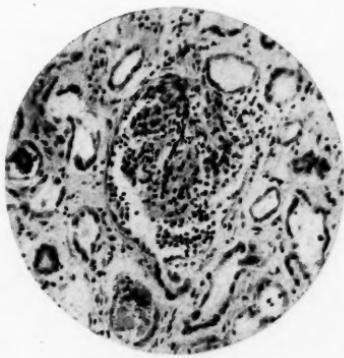
KIDNEY.

Acute capsular glomerulonephritis. Numerous polymorphonuclear leucocytes in the somewhat dilated capsular space.

lymphocytic infiltration of the connective tissue stroma. Regeneration of epithelium from the cells not killed is very active. Mitotic figures are often numerous. The first cells formed are stretched out very thin to cover the walls of the tubules. Later the cells thicken up and gradually become differentiated like their predecessors.

Lesions of this severe type commonly occur only after strong poisons. In the case pictured they followed abortion, perforation of the uterus, and streptococcus peritonitis. Similar lesions, but rarely so extensive, follow poisoning with corrosive sublimate.

The more common form of this lesion is less acute and extensive so far as necrosis is concerned, but the inflammatory reaction is usually much more marked: in fact, it often more or less completely masks the primary injury, especially if the process is seen in the later stages of repair.

This form of tubular nephritis follows such acute diseases as scarlet fever, diphtheria and measles. It does not occur early in such a disease, but only after ten days to several weeks. It is characterized by hydropic and hyaline change and by necrosis of the epithelial cells lining the convoluted tubules. The necrosis is rarely extensive in any one place. It is moderate in degree and more or less scattered. But the process of degeneration and necrosis is continuous for some time. On this account the inflammatory reaction is usually prominent. It consists of serum, fibrin and polymorphonuclear and endothelial leucocytes within the tubules which are often considerably dilated. Hyaline casts are also frequently present. In addition, the intertubular tissue is infiltrated with numerous lymphocytes including plasma cells and often also with small numbers of endothelial leucocytes and an occasional eosinophile. The infiltration with lymphocytes is usually the most prominent and characteristic feature of the lesion. On this account the term acute interstitial non-suppurative nephritis has been applied to it.

CAPSULAR GLOMERULONEPHRITIS.

This term is applied to an inflammatory reaction to toxins taking place within the capsular space around the glomerulus. The reaction may consist of several different elements, of an exudation of serum containing albumen, of an immigration of polymorphonuclear and endothelial leucocytes, and of a proliferation of the epithelial cells lining the capsular space. This reaction may be complicated by hemorrhage or by the formation of fibrin. According as one element or another predominates, the terms exudative or proliferative capsular glomerulonephritis are used. When hemorrhage occurs it is usual to say acute hemorrhagic nephritis without reference to the real lesion which underlies it. The various types of reaction depend on differences in the character and strength of the toxins brought to the glomerulus and excreted from it.

Exudative Type. When the reaction is exudative the fluid portion for the most part flows away with the urine. Only the fibrin which forms out of it and the cellular elements tend to remain. Within the dilated capsular space polymorphonuclear leucocytes may be present in small to large numbers according to the activity of the reaction. Many of these leucocytes pass into the tubules where some of them may undergo necrosis on their way to the pelvis of the kidney. Endothelial leucocytes are found in the exudation only in very small numbers; occasionally one of them will contain in its cytoplasm a polymorphonuclear leucocyte. Fibrin may occur as a delicate meshwork or in dense hyaline masses.

The exudative type of reaction is usually complicated by more or less proliferation and desquamation of the capsular epithelium, both from the parietal wall of the capsule and from the surface of the tuft. The cells from the latter situation often present a tailed appearance just as the cells
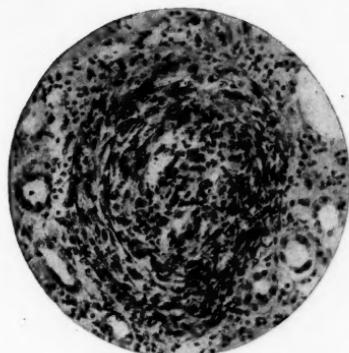
KIDNEY.

Acute capsular glomerulonephritis. Capsular space distended and filled with proliferated epithelial cells. One mitotic figure present along outer border of upper left quadrant.
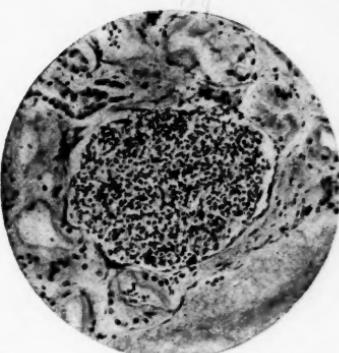
KIDNEY.

Acute intracapillary glomerulonephritis. The capillaries are distended with polymorphonuclear leucocytes.
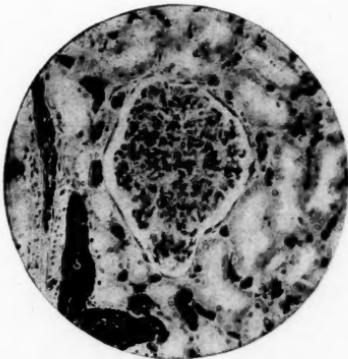
KIDNEY.

Acute intracapillary glomerulonephritis. The capillaries are distended with endothelial cells and leucocytes. One lobule of the tuft is forced into the beginning of the tubule.
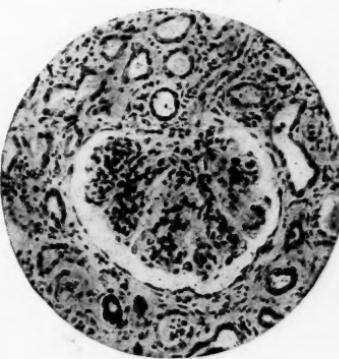
KIDNEY.

Subacute intracapillary glomerulonephritis. Lobulation of the tuft is well marked. The capillaries are distended and occluded with endothelial cells and leucocytes.

do in the deeper layer of the pelvis of the kidney. After desquamation the cells tend to assume a more or less spherical shape with an eccentrically situated nucleus and resemble endothelial leucocytes; but they are smaller, are not phago- cytic for other cells, and have the peculiarity of applying themselves to the surface of any fibrin formed in their neighborhood. These cells like the polymorphonuclear leucocyte often pass into the tubules, sometimes in large numbers. When numerous and packed in the capsular space these cells become flattened.

Proliferative Type. In many cases of capsular glomeru- lonephritis the reaction consists chiefly of proliferation and desquamation of the epithelial cells lining the capsular space. Mitotic figures are found in sufficient numbers (frequently two in a single section through a glomerulus) to account for all the cells formed. They occur in cells lining the parietal wall and covering the tuft and also in all layers of the masses of cells which collect together as the result of desquamation. These cells do not proliferate on account of injury to other epithelial cells adjoining them, as occurs in tubular nephritis where simple regeneration takes place, but because they are needed to counteract, probably by means of the production of an antitoxin, the toxins which filter through the wall of the tuft. They play the part acted elsewhere by the endothelial leucocyte. No analogous reaction, at least to anything like the same ex- tent, on the part of epithelial cells seems to occur in any other part of the body.

These desquamated cells when numerous form a crescen- tic mass within the capsular space with the thin edge towards the base of the tuft where the vessels enter and leave, and with the thickest part usually opposite the be- ginning of the tubule which they more or less completely occlude. Frequently the mass of cells projects for some distance into the tubule. The cells when numerous appear

flattened, probably from pressure, although the polymor-
phonuclear leucocytes among them preserve their spherical
and ameboid forms.

Fibrin is often associated with these cells in the form of
delicate fibers and sheets which run everywhere between
them, or as solid masses.

It is possible to conceive of the leucocytes and proliferated
epithelial cells disappearing entirely from the capsular space
when the purpose for which they are collected there is
accomplished, and of the glomerulus regaining its normal
function. As a rule, however, this return to the normal
condition is prevented owing to the formation of fibrin.
As soon as fibrin appears in the capsular space it stimulates
the fibroblasts in the tuft and in the capsule, wherever it
happens to touch them, so that they proliferate and grow
into it and organize it just as occurs elsewhere in the body
when fibrin is formed. Collagen fibrils take the place of
the fibrin. The epithelial cells which lined the surface of
the fibrin thus come to line the connective tissue. In this
way the capsular space may be divided into a number
of small epithelial lined cavities resembling glands. The
process is analogous on a small scale to what takes place in
the pleural cavity in the organization of a fibrinous exu-
date with the resulting formation of solid and stringy fibrous
adhesions, and gland-like cavities. In time the epithelial
cells more or less completely disappear and the newly
formed connective tissue contracts squeezing the tuft in a
strangle hold which destroys its power of functioning and
obliterates the capsular space.

In other capsular spaces the connective tissue grows very
early in between all the cells and no gland-like cavities re-
sult when organization takes place. In still other capsular
spaces the fibrin has been deposited irregularly in masses so
that the resulting fibrous tissue affects only a small part of
the capsular space; the rest is normal.

INTRACAPILLARY GLOMERULONEPHRITIS.

This term is applied to the reaction to toxins acting within the capillaries of the tuft. Sometimes the reaction is limited sharply to these vessels; at other times more or less toxin passes into the capsular space and occasionally into the tubules and leads to a reaction there also.

The reaction within the glomerulus may be evidenced by the formation of fibrin or by the accumulation of polymorphonuclear and endothelial leucocytes. Each of these elements may occur by itself or they may be variously combined. As a rule fibrin occurs in the most acute lesions, polymorphonuclear leucocytes in the less acute lesions, and endothelial leucocytes when the process is comparatively slow. The nature of the toxins probably plays some part, however. Occasionally eosinophiles are present.

Rarely the formation of fibrin within the capillaries of the glomerulus is the only striking evidence of a lesion in the kidney. The fibrin may occur in threads and networks or in solid masses and more or less completely occlude the vessels. It is probably due to a strong toxin causing direct injury (necrosis) of the capillary wall.

A lesion easier to understand consists of the accumulation of polymorphonuclear leucocytes in large numbers within the capillaries so that many or all of the vessels are distended and plugged with them. As a result, the glomeruli are considerably enlarged and the number of nuclei appearing in a section through one of them may be several times as many as normal.

Endothelial leucocytes often occur in various proportions in connection with the polymorphonuclear leucocytes. When the reaction within the glomerulus is not very acute and intense, however, the cell accumulation is limited almost entirely or even exclusively to the endothelial leucocytes. Some of these leucocytes are unquestionably brought

by the blood stream. Most of them, however, are derived directly by proliferation and desquamation from the endothelial cells lining the capillaries. Mitotic figures are by no means uncommon in the earlier stages of the lesion.

The endothelial cells and leucocytes distend and more or less completely occlude the capillaries and many of them exhibit ameboid forms. Very rarely they show phagocytosis for polymorphonuclear leucocytes. Eosinophiles are often associated with them; one to four and even as many as ten may occur in a section through a single glomerulus.

As a result of the accumulation of endothelial leucocytes in the capillaries the glomeruli appear more or less enlarged and in stained sections they are seen to contain many more nuclei than normally. Not infrequently a part of a lobule of the tuft will project from the capsular space into the beginning of the tubule. Usually the capsular space appears obliterated.

When the reaction is distinctly intracapillary in character, and the lesion is in its early stages, the normal lobulation of the tuft is usually more or less completely obscured because the dilatation of the capillaries forces the lobules close together.

Repair. When the toxins are strong and the reaction is intense so that fibrin and leucocytes occlude the capillaries more or less completely, death may occur from uremia in a few days or weeks. When, however, the toxins are mild and their action is prolonged, certain changes of a reparative nature gradually take place in the tuft. The fibroblasts forming the supporting walls of the capillaries, owing probably to some effect of the toxins, are stimulated to increased activity, possibly to proliferation; or it may be only a process of regeneration. At any rate the effect is that the collagen fibrils are increased in amount at the base of the tuft and running through the center of each lobule. As the connective tissue thickens and contracts the lobules
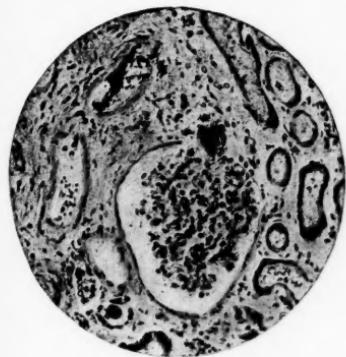
KIDNEY.

Vascular nephritis (arteriosclerosis). The afferent artery is almost occluded by thrombus formation.

KIDNEY.

Vascular nephritis. Sclerosed glomeruli and blood vessels, atrophied tubules, contraction and relative increase of connective tissue, infiltration with lymphocytes. Dilatation of some of the persisting tubules.

KIDNEY.

Acute infectious nephritis (pyelonephritis). Collecting tubules in pyramid filled with polymorphonuclear leucocytes which are also numerous between the lining epithelial cells and in the intertubular tissue.
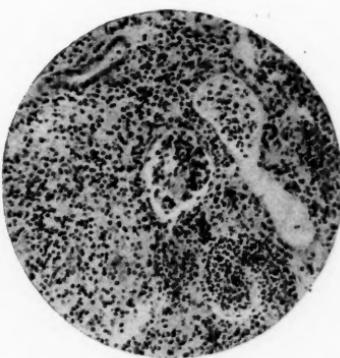
KIDNEY.

Infectious nephritis. Many polymorphonuclear leucocytes in the tubules and between the lining epithelial cells; many lymphocytes in the intertubular tissue.

are drawn apart so that at this stage, sometimes called subacute glomerulonephritis, the glomeruli are very distinctly and even prominently lobulated. Capillaries can be made out in them only here and there. As further contraction takes place the capillaries are completely obliterated and the lobules shortened and approximated so that the tuft is finally reduced to a small spherical, non-vascular mass of hyaline connective tissue containing a few fibroblasts. It has become a sclerosed glomerulus. This slow process of repair terminating in sclerosis of the glomeruli lasts sometimes for weeks and months.

VASCULAR NEPHRITIS (ARTERIOSCLEROSIS).

The primary lesion in vascular nephritis is located in the blood vessels, especially in the smaller arteries of the cortex and in the capillaries of the glomeruli. The lesion is similar in character to that which occurs in the aorta and other blood vessels in general arteriosclerosis and is a part of the same general process. It is a retrograde process characterized by the presence of much fat in the injured cells. The cells most affected are the fibroblasts beneath the lining endothelium. In addition, however, smooth muscle cells if present are also often involved, and not infrequently the lining endothelium itself is ultimately affected. Fat set free by necrosis of any of these cells is taken up by endothelial leucocytes. Necrotic fibroblasts are replaced by regeneration in excess so that the vessel walls are thickened and the limina narrowed. The elastic tissue is produced in increased amount by the fibroblasts. The muscle cells may entirely disappear.

When the lining endothelial cells are destroyed, fibrin formation (thrombus) commonly occurs and produces partial to complete occlusion of the part of the vessel affected. Later the fibrin is invaded and replaced by fibroblasts. In this way irregular thickening and frequently occlusion of

the vessels is produced. The process is chronic, lasting usually over many years; it is also frequently intermittent; but in suitable cases all stages of the development of the lesions can be found.

As the result of occluded capillaries and arteries many glomeruli become in part or entirely sclerosed. Sclerosis of a glomerulus is followed by atrophy and disappearance of its subtending tubule, and by contraction and hence thickening of the surrounding connective tissue.

The primary vascular lesion is diffusely and irregularly distributed throughout the kidney and may in time affect many glomeruli, thereby causing destruction of a large part of the kidney involved. It is evidently toxic in origin, but as it often leads, by narrowing the lumina vessels, to interference with the blood supply in adjoining parts of the kidney, secondary lesions due to lack of nutrition arise. It is probable that the two types of lesions cannot always be distinguished from each other.

INFECTIOUS NEPHRITIS.

Infectious nephritis (the only lesion of infectious origin considered here) is the term applied to a diffuse inflammatory process in the kidney due to the immediate presence of organisms. It is most often caused by the colon bacillus, and infection, as a rule, takes place from the pelvis of the kidney, which has been invaded from the urinary bladder by way of the ureter. The organisms invade the tubules and ascend along them to the cortex, but they rarely invade the capsular space of a glomerulus. They produce an acute inflammatory reaction which is combined with more or less necrosis of the epithelium lining the tubules. The exudation consists of polymorphonuclear and endothelial leucocytes in varying proportions and of serum and fibrin. They collect in the tubules and distend them.

KIDNEY.

Amyloid infiltration of the glomerular tufts and of the arteries in the kidney.
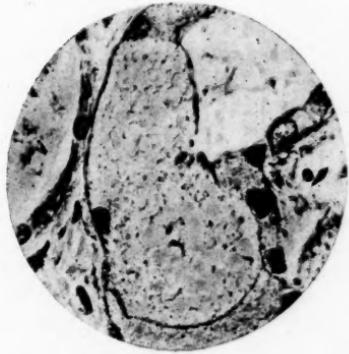
KIDNEY.

Hyalin in epithelial cell lining a tubule.   This variety stains faintly.   It often
escapes owing to rupture of the cells and forms waxy casts.

XUM

Frequently a similar exudation is present in the intertubular connective tissue and has mingled with it numerous lymphocytes and plasma cells. An inflammatory process such as this may extend in narrow or broad, gradually widening bands from the pelvis to the capsule of the kidney or invade it more or less diffusely and extensively. Sometimes this fairly mild process is complicated by more or less extensive hemorrhage and by abscesses due to areas of necrosis of tubules and surrounding tissue, followed by softening. At other times the infectious organism is more virulent, and necrosis and softening are more extensive, so that abscesses and suppurating tracts form the most obvious lesions (suppurative nephritis, chronic pyelonephritis, surgical kidney).

Infectious nephritis may undergo repair at any stage of the process provided the infectious organism is killed off. This may happen in some foci and not in others, or it may occur throughout the kidney. Lesions in all stages of repair may frequently be found in the same kidney. The final result depends on the amount of injury done. Sometimes the tubules are completely restored by regeneration of the epithelium. At other times the tubules are narrow and the epithelium but little differentiated. Occasionally they are completely destroyed. The glomeruli may remain normal or be transformed into small masses of dense fibrous tissue. The intertubular connective tissue is usually more or less increased in amount, probably as the result of regeneration following injury, and as a rule contains a varying number of lymphoid cells.

Infectious nephritis is probably more common than is generally supposed. It occurs both in children and in adults, and frequently terminates in repair. It very often complicates other lesions of the kidney especially vascular nephritis and amyloid formation.

Its recognition is important because in its healed stage it

is often mistaken for some form of toxic nephritis, especially for the vascular variety or so-called arteriosclerosis.

AMYLOID KIDNEY.

There is still one type of lesion which requires consideration, namely the amyloid kidney. Possibly it belongs in the group labeled toxic nephritis. Amyloid seems, without much question, to be an abnormal product of the fibroblasts. In the kidney it is formed first in the glomeruli and the blood vessels and later in the connective tissue generally between the tubules. Early in the process the kidney is enlarged owing to edema and colloid formation in the renal epithelium. In the later stage, however, when the amyloid deposit is marked, the tubules atrophy and disappear to a large extent and the kidney is diminished in size and much sclerosed. Whether the sclerosis is due to the same cause as the amyloid or follows as a result of the amyloid formation is not evident. More study is required on this point.

ARTICLE IX.

THE SIGNIFICANCE OF URINARY ACIDITY IN NEPHRITIS.

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DELIVERED JUNE 10, 1913.

THE SIGNIFICANCE OF URINARY ACIDITY IN NEPHRITIS.

THE functions of the kidney are numerous and undoubtedly to a large extent interdependent. Under normal conditions the organism depends mainly on the kidney to regulate the acid-base equilibrium, osmotic pressure and water content, and to eliminate the end products of nitrogenous metabolism as well as many other less well-known substances. In experimental and pathological states a great variety of additional functions may be called into play. The results of the studies of the functions of the kidney under experimental conditions, though frequently difficult of interpretation, have their particular value. It is the purpose of this paper to report certain significant facts concerned with that normal and very important function of the kidney which has to do with the regulation of the equilibrium between acid and base in the human organism with especial reference to nephritis.

Except under unusual circumstances the acid products of metabolism exceed the basic. Unless the excretion of the acid products is carefully regulated acidosis results and manifests itself in depletion of sodium bicarbonate from the blood. Except for carbonic acid which is excreted in the lungs, it is the work of the kidney to remove these acid products that the necessary constant equilibrium between acid and base in the body may be maintained. The kidney performs this function by removing a more acid fluid than the blood in which acid radicals are partially combined with ammonia. The efficiency of the kidney in performing this process depends on the intensity of urinary acidity.[1]

In our study of acid excretion three factors have been separately determined.

1. Urinary acidity (hydrogen ion concentration) as described in an earlier paper.[2]

2. Excess acid as measured by titration of the urine with sodium hydrate to the reaction of blood using neutral red as an indicator.[3]

3. Ammonia, determined by Folin's New Method.[4] The daily amounts of acid and ammonia are recorded as one-tenth normal solutions and for the total acid are additive.

The intensity of urinary acidity has been measured in over 3000 samples of urine from six hundred to seven hundred different individuals, one hundred and fifty of which were normal. In normal individuals there was considerable variation in the acidity, the general average being about twenty-five times that of normal blood while in many pathological cases there was a marked increase over the normal. Especially was this true in nephritis. In acute and chronic nephritis the acidity averaged between one hundred and twenty-five and two hundred and fifty times that of blood as compared with normal average of twenty-five. In nephritis and some other pathological conditions the acidity is persistently high throughout the twenty-four hours, while in normal individuals it is subject to considerable variation. We have never found a significant diminution of acidity in pathological cases nor in any case normal or pathological, a degree of alkalinity greater than that of blood, save after the administration of alkali or other experimental interference.[5]

We have confirmed the observation of Sellards[6] upon the action of ingested sodium bicarbonate upon the reaction of the urine. In all normal and many pathological individuals the small amount of one dram of sodium bicarbonate produces a marked lowering of the urinary acidity within one

hour, while on a variety of pathological cases large quantities of alkali were without effect upon the reaction of the urine. These cases included many nephritics, also cases of pleurisy with effusion, primary and secondary anemias, pneumonia, in addition to conditions where beta-oxybutyric acid is formed. Further, we find that such cases when once the urine has been made alkaline, upon discontinuing the alkali until the urine is once more acid, respond to the alkali in a normal manner. This observation leads us to believe that Sellards's term "tolerance" is inexact, that the phenomenon is due to a drain of alkali from the body and is in fact a real test for acidosis. These observations extend to a much larger variety of cases in which more accurate estimations of urinary acidity were made than has been observed by Sellards, and were made before we were aware of his work. Our observations lead us to believe that alkali as a therapeutic measure is indicated in many conditions not previously suspected, also that when alkali is given for whatsoever cause the effect on the urine should be carefully watched. The reaction of the urine should never be pushed below that of blood for we have found in normal individuals that when this occurs not infrequently a well-marked albuminuria may result.

The quantity of acid excreted in the urine (excess of acid plus ammonia) has been studied in sixteen normal individuals and thirty-five cases of nephritis. The two fractions of acid excretion appear to vary independently though they are likely to be more nearly parallel in normal cases. When the two quantities are computed in cubic centimeters of a one-tenth solution the ammonia is greater than or equal to the acid. In chronic glomerular nephritis the relation is reversed, the ammonia occasionally being less than one-third the amount of acid excreted. The ammonia appears to be an index of the degree of acidosis only in those cases where beta-oxybutyric acid is produced.

In nephritis the relation between the intensity of urinary acidity and the total quantity of acid excreted varies greatly from normal. This variation is most marked in the more advanced cases of chronic glomerular nephritis. The intensity of urinary acidity is much greater than normal one hundred to two hundred fold while the total acid excreted is much less, not infrequently one-half to two-thirds. This relation seems to be much less disturbed in acute nephritis and individuals with the arteriosclerotic type of kidney. The relation between urinary acidity and total quantity of acid excreted appears to provide an index of the efficiency of the kidney in carrying out the important process of acid excretion. This "functional test" possesses the advantage that it involves no experimental interference.

We have reached the conclusion that mild states of acidosis not infrequently occur in nephritis, and other unsuspected cases and that the therapeutic use of alkali (in such quantity as to reduce the urinary acidity to that of blood) is often desirable. We also believe that the deviation from the normal of the kidney function in acid excretion is important both in differential diagnosis and prognosis.

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ARTICLE X.

CLINICAL FUNCTIONAL TESTS, METHODS.

The Place of the Phenolsulphonephthalein Test in Nephritis.

By Edward L. Young, Jr., M.D.,
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Delivered June 10, 1913.

CLINICAL FUNCTIONAL TESTS, METHODS.

ANY clinical test to be of widespread value must have among other qualities the following essentials: first it must be easy to use both as regards technique and time required so that any practitioner can use it without complicated and expensive apparatus and without using up more time than he can afford; second, it must be harmless and painless to the patient; third, it must give consistent and accurate information of definite value in diagnosis, prognosis and treatment. This, test perhaps more than any other now in use fills all of these requirements. The only apparatus necessary is a hypodermic syringe measuring accurately in cubic centimeters; some of the drug which comes ready to use; some 25 per cent NaOH; some form of colorimeter which may vary in kind from the simple but clinically accurate home-made affair to the expensive imported instrument. The simplest form is a series of equal sized tubes containing slightly alkaline solutions of the drug varying from 5 to 50 per cent in strength, and another tube of the same size in which to put the solution to be measured; and lastly some vessel in which the urine obtained can be diluted to 1 liter. The technique is as follows:

One centimeter of the solution containing 0.6 gram of the drug is injected into muscles of the thigh; then one of two procedures may be followed; first the amount of urine during the next two hours may be collected, made alkaline with NaOH to bring out the color, diluted to one liter and the amount of drug measured by comparing its color with the color of the standards, since the amount of drug is in proportion to color. If there is any reason to suppose the

patient does not empty the bladder a catheter must be used. Second, a catheter may be placed in the bladder and the urine allowed to drain into a receptacle containing some NaOH and the time of appearance, as shown by a pink color, is noted. Then the urine in the hour following the appearance is collected, diluted and the drug measured. By the first method the average normal output is 70 per cent, and by the second 40 per cent, of the amount injected with a time of appearance of from 8 to 15 minutes. Any fall in output is in proportion to a loss of functional ability of the kidneys at that time. The time required depends on which method of procedure is used. If the first is used and no catheterization is necessary then the drug can be injected in a few seconds and the amount collected by the patient, and later at his convenience, the physician can dilute, alkalinize and estimate all in a few minutes. The second method requires a little more time but is likewise a little more accurate.

The drug is absolutely harmless and painless to the patient in every way and causes no more local reaction than the insertion of the needle itself.

As regards the last requisite there has never been any question but that the results are accurate and consistent, and the whole question lies in the value of these results in diagnosis, prognosis and treatment. That this method of estimating the kidney condition and its ability to stand the strain of operation, especially any operation involving the urinary tract, is of the very greatest value, has been proved beyond a doubt and the right interpretation of and reliance on this test has been the means of lowering the mortality in several of these operations and especially in prostatectomy. Its place in surgery is fairly well fixed and no one who has had any experience with this test would operate in the face of a low output without studying the case very carefully.

The place of this test in medical nephritis, if I may use that term, is perhaps not so definite but I believe that it

has its place and is of greater value than it is given credit for and might be of even more use, this value being not to say whether the glomeruli or tubules are involved but how much work the kidneys are capable of doing.

I shall give a few of the cases in which its results have been checked up either by autopsy or by the future conditions of the patients.

CASE I. A painter of 32 came with the following story; had been off color all winter, increasing shortness of breath, edema of legs at times, attacks of vomiting in the morning, had had a cough most all winter and had caught cold easily. He is an anemic and has a blood-pressure of 200 mm. Urine as follows,—normal, acid, 1012, trace of albumen, no sugar. Sediment shows casts, a few round and squamous cells, few red blood cells. While in the hospital he rapidly improved, blood pressure came down to 160 mm. amount of urine rose and albumen lessened. But the "red" test showed that no drug appeared in the urine for 50 minutes and the amount during the next hour was too small to measure. The last note in the record is as follows: "the patient now has no symptoms and is going home. There is a marked discrepancy between the test and the clinical findings." About six weeks after discharge I went to see how he was getting along and found he had been dead for nearly a month.

CASE II. A man of 72 entered the hospital with a general suppuration of the urinary tract: in poor condition. He got worse, began to hiccough, got nauseated, failed steadily and from his symptoms was thought to be dying of uremia. The "red" test showed a delayed appearance to 30 minutes but an output of 26 per cent in the next hour. At autopsy his kidneys were poor but according to the pathologist "compatible with a fair degree of work." But his heart was in very poor condition showing both myocardial and endocardial changes of high degree and it was to this that death was due.

CASE III. A man of 42 enters the hospital with a diagnosis of "Chronic Glomerulonephritis, Cardiac Hypertrophy and Dilatation and Hemiphlegia." The "red" test showed

a time of output of 19 minutes and an amount during the first hour of 9 per cent. Patient gradually failed, got drowsy, irrational and died. Autopsy showed, combined weight of kidneys 230 grams, capsule strips leaving rather pale granular surfaces. On section the tissue is quite firm, the cortices and pyramids are made out and cortex measures 4 to 5 mm. The cortex shows obscuration of the markings, is somewhat flint-colored and shows in places minute to small yellowish gray short streaks and areas. In a few places the cortex shows mottling with dark brownish red areas. The cut ends of the vessels are slightly prominent.

There are one or two small cysts in each kidney.

Microscopical Examination. Marked arteriosclerosis with atropic changes in the tissues. Considerable hyaline degeneration of the smaller arteries, hyaline thrombi in some of the capillaries and some of the glomeruli. In other words a pathological condition apparently entirely consistent with the test.

There have been other cases in all of which the test has told the truth but these serve to illustrate the point. The use of this test in cardiorenal cases has helped and I think always will help to place the blame more accurately on the organ more at fault.

In coma of doubtful origin it will cast a strong vote for or against uremia.

In acute nephritis it is of less value, as very often a fairly sick patient will eliminate a considerable amount of the drug.

In chronic nephritis, inasmuch as a fairly low output is not incompatible with a considerable length of life if the kidneys can be kept in a state of compensation, some additional fact must be found, which, coupled with this test will give a more accurate prognosis as regards time.

To conclude — the phenolsulphonephthalein test comes nearest to fulfilling all the requirements of a clinically valuable functional test in that it is easy to use, is harmless to the patient, and gives accurate and consistent knowledge of

the actual working ability of the kidney, a fact that the practitioner wants more than the knowledge of whether the glomeruli or tubules of the kidney are affected.

In surgery it already has a recognized place.

In medicine it has a certain value which will increase with the increase in use.

ARTICLE XI.

TESTS FOR RENAL FUNCTION BASED UPON THE SELECTIVE EXCRETORY ACTIVITIES OF THE KIDNEY.

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DELIVERED JUNE 10, 1913.

TESTS FOR RENAL FUNCTION BASED UPON THE SELECTIVE EXCRETORY ACTIVITIES OF THE KIDNEY.

THE association between clinical and post-mortem findings in nephritis has never been clearly defined. In 1905 Friedrich Müller suggested trying to correlate the signs of abnormal renal function as shown by various tests, with the different types of nephritis found during life and at autopsy. Since that time much work on the more exact study of renal function has been done, originating mainly from Schlayer and his co-workers.

Tests have been devised to study individual functions of the renal tubules and of the vessels of the glomeruli, based on the assumption that different portions of the renal structure have selective excretory activities. It must be emphasized that such are tests for renal function alone and cannot be made to prove the presence of constant anatomical lesions. By their use, however, renal physiology under pathological conditions can be studied more accurately than by usual clinical observations. It is the purpose of this paper to describe the technic of such tests and to state how information obtained by their use may be of value in the diagnosis, prognosis, and treatment of nephritis.

While under observation the patient is ordered a constant diet containing known amounts of fluids and salt. The total amount of fluid and sodium chloride excreted is followed from day to day. Experiments have shown that water and lactose when injected intravenously are put out mainly through the action of the glomerular vessels while

sodium chloride and potassium iodide come to the urine through the tubules.   On different days an intravenous injection of lactose is given, or ten additional grams of sodium chloride by mouth, or one-half a gram of potassium iodide by mouth.   The manner of excretion of these substances is observed.

Two and one-half grams of pure lactose are dissolved in twenty-five cubic centimeters of freshly distilled water, placed in small cotton stoppered Erlenmeyer flasks and pasteurized for four hours daily on four successive days at a temperature between 75 to 80° C.   By this method the dose used is slightly over 2 grams of the sugar in twenty cubic centimeters of water.   A fresh solution is used for each injection.   Unless the lactose solution is so carefully prepared and sterilized, severe chills and other constitutional symptoms may follow its administration.   After injection all the urine is collected at the end of four hours and every hour or two thereafter to twelve hours.   Each specimen is tested for the presence of sugar with Nylander's reagent, using constant amounts of urine, solution, and a constant length of time for boiling.   In this way excretion time is determined.   Polarimetric readings must also be made to quantitate the total amount of sugar excreted.   Normally 60 per cent or more of the dose injected is regained in from four to six hours.   Abnormality in excretion, both as for time and amount, affords an index to the degree of glomerular functional disturbance.

In health, water is excreted in amounts of about two-thirds of the fluid intake.   When the glomerular function is abnormal, water excretion as a rule, is markedly increased or diminished for long periods of time.   The polyuria is considered to be due to a hypersensitive condition of the glomerular vessels by which they respond continuously to the small amounts of diuretic substances contained in food. The oliguria, on the other hand, is due to a torpid condition

of these vessels as a result of which they are unable to excrete the usual amount of fluid. Which of these conditions exists is determined by the ratio of fluid output to intake. Further proof is found in the kidney's response to the diuretic stimulation of sodium chloride.

The excretion of salt is accomplished chiefly by the concentrative powers of the tubules. Normally in large amounts it is put out by one of two methods. If the sodium chloride is given without extra water it is excreted almost completely within twenty-four hours by increased concentration in the urine; if given with additional water it is excreted partially by increased concentration and partially by an increased amount of urine. In severe tubular injury with normal vessels added salt is retained in the body since the tubules are impermeable. Their functional capacity is determined by following in the urine, variations in the concentration curve of sodium chloride after it is ingested in large amounts without extra water. Salt is, however, under certain conditions a diuretic. In that type of glomerular injury characterized by hypersensitive vessels the added chloride produces an increased urinary outflow. Then it is excreted mainly in the excess of water, its concentration in the urine being increased or not depending on the condition of the tubular function.

Thus there are two distinct types of abnormal salt reaction. In the first added salt is not put out because the tubules are unable to concentrate it sufficiently and because the glomeruli are not hypersensitive. In the second added salt is excreted promptly, mainly by diuresis, in part by increased concentration in the urine, because the glomeruli are hypersensitive, and the added salt acts as a diuretic. Between these two extreme types of salt excretion are variations depending upon differences in tubular function on the one hand, and glomerular function on the other.

Potassium iodide is excreted by the tubules. For the

dose given the normal elimination time is sixty hours or
less. The urine is tested for the presence of the drug at
the end of forty-eight hours and every six hours later until
the reaction for it is negative. Iodide in the urine is de-
termined conveniently by Sandow's test. Two cubic centi-
meters of 2 per cent sodium nitrate solution, 2 c.c. of 10
per cent H_2SO_4 and 30 c.c. of urine are mixed. To this is
added a few cubic centimeters of chloroform. The whole is
shaken. Purple or violet color appears in the chloroform if
iodine is present. Theoretically the more marked the
degree of tubular disturbance, the more marked the delay
in iodide excretion. Various observers however have found
this test of little practical value in the determination of
renal function.

On the whole by using these tests in the fashion outlined,
it is possible to discover abnormalities in function on the
part of the tubules and glomerular blood vessels of the
kidney. Abnormal tubular function is shown by the in-
ability of the kidney to increase the concentration of salt in
the urine when an excess of salt is added to the diet and by
a delay in the excretion time of potassium iodide. Abnormal
glomerular function is shown by the inability of the kidney
to excrete lactose in the usual time and quantity. Further-
more abnormal glomerular function is of two types. The
vessels are either hypersensitive as shown by a constant
polyuria increasing in response to the vascular stimulus of
salt, or hyposensitive as shown by a constant oliguria.
The tests are of considerable quantitative value. In general
the severity of functional derangement shown by them cor-
responds with the clinical and anatomical severity of the
disease. Cases studied by these methods can be grouped
functionally into glomerular nephritides, tubular nephritides
and a mixed form which shows functional derangement of
both systems. The last group contains the majority of
cases which are observed clinically.

The practical value of these tests lies in the ability afforded by them for more accurate diagnosis, prognosis and treatment of nephritis than can be attained by clinical observation alone. In many cases by their use it is possible to acquire positive evidence of a severe derangement of renal function before any clinical manifestations develop. Thus the tests are of value for the early diagnosis of nephritis. By repeating them at intervals over a long period of time it is possible to follow the progression of the disease through various stages of functional change. In this way, whether the renal function is returning to normal, remaining stationary or becoming worse can be determined. Thus the tests give valuable prognostic information. Finally, to some extent, the results of these tests offer a rational basis for treatment. It has been shown that the hypersensitive type of vascular lesion associated with polyuria is less severe than the oliguric type. Certain cases of the latter group can be stimulated into reactivity by small doses of caffein or digitalis derivatives given over a long period of time. The beneficial effect of a salt and water poor diet on renal patients unable to excrete salt or water has been recognized previously.

In conclusion it must be emphasized again that the lactose, water, salt and iodide tests study renal function without regard for the specific anatomical lesion producing the effects. By the use of these tests it is possible to follow certain phases of pathological renal physiology. Information obtained in this way is of greatest value in the early diagnosis of abnormal renal function. It may also be of value in prognosis and treatment.

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NITROGENOUS WASTE PRODUCTS IN THE BLOOD IN NEPHRITIS.

Their Significance and the Methods for Their Determination.

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AND

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NITROGENOUS WASTE PRODUCTS IN THE BLOOD IN NEPHRITIS.

URINE analysis though now developed to a comparatively high degree of perfection can furnish very little information concerning the actual retention of waste products in the body. Yet unless the physician can know the level of accumulation of such products in any given case of nephritis the treatment which he prescribes, particularly the dietetic treatment, must of necessity be indiscriminate.

For further progress in the study and treatment of nephritis it would seem to be absolutely necessary that blood analysis be introduced to supplement the analysis of urine. The old popular notion about "impure blood" is after all not entirely without sense for whenever the kidneys fail to do their work adequately the products which are left behind must accumulate in the blood as well as in the tissues. Theoretically the importance of chemical blood analysis in connection with nephritis has been recognized for a long time but no one so far as we know has made any sustained effort to devise suitable methods for such work. The literature on the subject though abundant and associated with the names of prominent clinicians is from a chemical standpoint as crude as was the literature on urine fifty years ago.

Recognizing the lack of suitable chemical methods for the determination of waste products in the blood we took up the subject about three years ago and have developed methods for the determination of the ordinary nitrogenous waste products, the total nitrogen, the urea, ammonia and uric acid. It would scarcely be suitable to take up your

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time with descriptions of the technical details involved in such analytical work for although intended for clinical work the methods can by no means be called clinical methods. It will, therefore, be sufficient to say that the problem which we had to solve was to find methods applicable to moderate quantities of blood, such quantities for example as are taken for the Wassermann reaction. By the help of certain color reactions (chiefly Nessler's reaction) we have solved the problem and now can determine all the products mentioned in about one ounce of blood. For the total (nonprotein) nitrogen and the urea the two most important determinations in nephritis we need only about five cubic centimeters of blood.

By the help of these new methods we have made a great many blood analyses during the past year, and among these there are about 50 cases of nephritis. Speaking on the basis of these 50 cases we can say that the accumulation of waste products in the blood varies between figures which are nearly normal to figures which are four or five times as large as the normal. As yet we have not found that any particular diagnosis corresponds to any particular degree of accumulation of waste products except that in cases of pronounced or threatened uremia the blood so far as our experience yet goes is invariably very high in waste nitrogen. There is no correspondence between the blood pressure and the degree of retention of the ordinary nitrogenous products included in our analyses.

One of the important questions to be solved by the help of blood analyses is the effect of low protein diets in the case of nephritic patients who suffer from an accumulation of unusually large amounts of waste products. It is *a priori* not clear whether damaged kidneys are capable even on low protein diets to eliminate the waste products down to the normal level of retention for it is conceivable that a certain concentration of the waste products in the blood

must be reached before any elimination can take place, and that this threshold of elimination is raised above the normal in nephritis. The results which we have so far obtained indicate that this is not the case. All the nephritic patients which we have yet examined on high and on low protein diets have shown that on the low nitrogen diets the accumulation of waste products sink and can be brought down to the normal level. In view of this fact it is clear that for a correct interpretation of figures obtained from blood analysis the total level of protein metabolism must also be known, in other words blood analysis must be accompanied by determinations of the total nitrogen in the urine.

Our analytical results have also revealed the fact that the retentions of urea and of uric acid do not go hand in hand. The urea retention is by no means always accompanied by an abnormal uric acid accumulation and considerable uric acid retention may occur without any considerable increase of the urea. These peculiar facts would seem to indicate that in some cases it is more important to exclude meat and other purin food than in others and that a low protein diet does not necessarily imply a meat free diet. It looks as though by blood analysis it should be possible to determine with a very fair degree of certainty what kind of diet is suitable for each particular case of nephritis. It is already well recognized that the salt content of the food must be regulated in some kinds of nephritis and it seems to us equally clear that similar unequal abilities exist with reference to the nitrogenous products and that in such cases more definite knowledge can be obtained by means of blood analysis than in any other way.

ARTICLE XIII.

NITROGENOUS WASTE PRODUCTS IN THE BLOOD.

Their Effect in Chronic Interstitial Nephritis.

By Malcolm Seymour, M.D.,
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Delivered June 10, 1913.

THE EFFECT OF NITROGENOUS WASTE PRODUCTS IN THE BLOOD IN CHRONIC INTERSTITIAL NEPHRITIS.

THIS work was undertaken to study the effect of high and of low proteid diet on patients suffering from Chronic Interstitial Nephritis, with increased arterial tension.

Fourteen patients were selected, each case having an arterial hypertension, persistent low gravity urine, with small amounts of albumen, and rare hyaline casts.

For five days the patients were given the regular hospital diet, which contained about sixty grams of proteid. At the end of this period the proteid content of the diet was increased and this diet maintained for seven days. By the sixth day they were given about one hundred and eighty grams of proteid daily. During the next period of eight days, the proteid was reduced, so that they were given very small amounts, the daily average for this period being about twelve grams.

The nitrogen content of the blood was measured at the end of the normal hospital diet period, and at the end of the high and of the low proteid diet periods.

Urinary nitrogen determinations were made daily, except on the days when the phenol sulphone-phthalein tests were made. These latter were made five times during the course of the experiment.

Out of the fourteen cases, eight showed an increase in the nitrogen content of the blood at the end of the high proteid period.

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Of these eight cases showing a nitrogen increase, six had edema of the face with puffiness of the eye-lids, and complained of nausea and headache. All of these patients vomited, and in each case refused food at the end of the sixth day. Two of the patients who showed the greatest increase in the blood nitrogen, had more marked symptoms than those showing a more moderate one.

Two cases showing an increase in the nitrogen, had no symptoms.

Of the six patients showing no increase in the nitrogen of the blood, one had only edema of the face, two had nausea and vomiting with slight edema of the face, two were drowsy, dull, and complained of headache. One patient showing no nitrogen increase, had no symptoms.

The effect of the blood pressure is difficult of interpretation, on account of the irregularity of the arterial tension under normal conditions, but it seemed to be an interesting observation, that of the eight patients showing an increase in the blood nitrogen, six showed a lowering of the blood pressure during, at the end, or slightly after the high proteid period. One case had no change in the blood pressure, and in another, the pressure became irregular.

Of the six patients showing no increase in the nitrogen content of the blood, two showed a simple irregularity, three no change, and one patient showed a lowering in the blood pressure.

There seemed to be no relation between the arterial tension and the low proteid diet during the eight day period the diet was continued. In some cases there was an irregularity, in some a rise, and in others a fall in the pressure; even though the nitrogen content of the blood was greatly diminished in every instance.

In the phenol-sulphone-phthalein tests, the excretion of the dye was decreased in every case, but here again there seemed to be no relation between the blood-nitrogen con-

tent and the excretory function of the kidney as measured by this test. This may be due to injecting the material in the gluteal muscle. Recent observations by Fromme and Rubner show that more constant results are obtained if the solution is given intra-venously.

I wish to thank Professor Folin for the privilege of collaborating with him in this experiment, and also thank Dr. Dennis for her assistance in making the many nitrogen determinations. To Dr. Fitz I also extend thanks for the help in making the phenol readings.

NITROGEN BLOOD

	House diet.			High protein.			Low protein.		
	Non prot N	Urea N	Uric acid	Non prot N	Urea N	Uric acid	Non prot N	Urea N	Uric acid
Case No. 10......	30	15	2.6	32	16	2.8	19	10	2.0
" " 5......	30	15	2.5	30	15	3.0	19	10	not done
" " 8......	40	18	1.9	40	20	2.7	21	11	2.5
" " 4......	39	18	3.0	62	45	3.9	30	15	2.7
" " 1......	44	26	1.7	44	24	2.7	19	10	1.7
" " 6......	50	28	2.7	58	40	3.3	23	12	2.0
" " 7......	30	14	3.0	37	20	2.9	20	11	2.1
" " 3......	50	28	2.2	82	67	3.9	26	12	2.3
" " 2......	28	14	2.5	30	15	2.5	20	11	2.6
" " 13......	49	25	2.6	48	23	2.6	22	10	1.8
" " 11......	27	14	2.6	30	16	2.8	20	11	2.3
" " 9......	38	20	2.2	37	20	2.3	23	11	2.0

URINE

April, 1913.

(Figures indicate grams of Nitrogen in 24 hours)

	House diet						High protein								Low protein								May
	9 to 10	10–11	11–12	12–13	13–14	14–15	15–16	16–17	17–18	18–19	19–20	20–21	21–22	22–23	23–24	24–25	25–26	26–27	27–28	28–29	29–30	30–1	
	Phenol-Sulphone-Phthalein Test	Blood	ood	"N"		Av.				Phenol-Sulphone-Phthalein Test	Av.								Phenol-Sulphone-Phthalein Test. Last blood taken.	Urine not examined		Av.
Case No. 1	8.4		5.1	7.4	8.4	44 / 8.0	7.4	7.5	8.1	8.4		12.4 / 03	44 / 15.0	10.2	9.8	6.6	6.0	4.4	4.2			19 / 2.9	5.6
" 2	10.1		6.7	11.4	9.9	28 / 11.1	9.8	11.1	11.3	10.6		14.4 / 82	15.3 / 03	12.5	10.8	10.9	6.3	2.4	3.8			20 / 2.8	6.1
" 3	7.4		6.8	9.4	10.3	50 / 9.8	8.7	9.1	9.5	11.5		11.7 / 62	11.1 / 82	10.5	6.7	7.5	4.9	3.3	1.9			26 / 2.4	4.4
" 4	11.1		10.5	6.4	7.8	39 / 8.7	8.9	8.3	13.1	9.6		14.1 / 30	13.6 / 62	11.7	8.5	7.7	6.1	5.6	4.8			30 / 3.5	6.0
" 5	7.3		5.8	6.4	9.2	30 / 7.9	7.3	8.2	12.0	12.5		10.1 / 58	9.6 / 30	10.4	7.7	9.8	5.3	4.7	3.4			19 / 3.5	5.7
" 6	7.8		5.7	7.8	8.5	30 / 12.2	8.4	8.4	8.5	12.0		11.1 / 37	10.0 / 58	10.0	6.7	6.9	4.5	5.7	4.3			23 / 2.3	5.0
" 7	13.9		10.5	11.1	9.3	40 / 9.5	10.8	8.9	9.9	15.5		13.2 / 40	18.3 / 37	13.8	2.5	8.4	6.2	4.6	3.4			20 / 2.1	4.5
" 8	9.7		9.9	9.7	9.2	38 / 8.4	9.3	8.9	10.3	12.6		11.2 / 37	9.7 / 40	10.5	7.9 / 11.5	11.5	5.5	3.5	2.7			21 / 1.3	5.4
" 9	7.0		5.1	9.0	9.0	30 / 7.8	7.2	9.2	8.2	10.8		11.3 / 32	10.6 / 37	10.0	7.4	9.0	5.3	7.1	3.3			23 / 3.4	7.1
" 10	15.0		5.6	8.5	9.5	27 / 9.6	9.6	11.5	12.3	14.2		13.0 / 30	14.8 / 32	13.1	7.0	7.5	4.8	4.6	4.2			19 / 3.4	5.2
" 11	4.8		5.1	5.4	9.8	49 / 7.4	6.5	7.0	9.6	9.0		13.0 / 48		9.6	7.0	7.8	3.5	2.6	3.3			20 / 2.0	4.3
" 13			5.4	11.2	8.8	12.0	9.3	10.1	13.7	14.8		16.2 / 48	18.7	14.7	8.7	10.4	6.5	5.9	5.2			22 / 4.4	6.8
" 14			6.2	5.7	10.8	10.1	8.2	9.0	9.7	7.8		9.2	10.8	9.3	7.7	10.5	5.0	2.2	4.9			4.6	5.5

PHENOL-PHTHALEIN TESTS.

	April 10.		April 15.		April 19.		April 22.		April 28.	
	1 hour.	2 hours.	1 hour.	2 hours.	1 hour.	2 hours.	1 hour.	2 hours.	1 hour.	2 hours.
Case No. 1.	13	44	trace	12	none	22	16	36	10	35
" " 2.	trace	12	9	34	8	23	10	lost	10	30
" " 3.	14	30	9	21	14	28	13	26	19	35
" " 4.	4	35	33	no spec.	12	23	10	30	10	29
" " 5.	13	23	13	35	8	16	10	18	10	20
" " 6.	trace	9	trace	14	10	20	6	17	12	28
" " 7.	trace	12	trace	13	12	45	13	33	12	28
" " 8.	10	26	9	22	20	38	7	26	35	45
" " 9.	25	47	9	34	10	29	15	34	10	37
" " 10.	6	18	6	29	20	37	20	39	20	33
" " 11.	trace	7	trace	2	no spec.	26	11	31	8	24
" " 12.	38	61	14	39						
" " 13.	trace	25	trace	9	6	31	19	39	25	50
" " 14.	13	no spec.	trace	no spec.	trace	15	no spec.	25	5	15

Case No. 1

April   *Name* R. E.   May   Case No. 3

House diet

High Proteid

Edema of face and eyelids esp.
Edema face, nausea, vomiting, headache,

Low Proteid

Medium Proteid

P.M. A.M. Nitroglycerine
Sodium Nitrite

BLOOD PRESSURE

PROTEIN INTAKE GRMS.

URINE

NON-PROT. "N"

UREA "N"

BLOOD

BLOOD

PHENOL TEST

March   *Name* K. M.

BLOOD PRESSURE

PROTEIN INTAKE

NON-PROT. "N"

UREA "N"

URINE

Nausea, vomiting, headache.

Refused food.

March Name K. M.

34

42

43

44

61
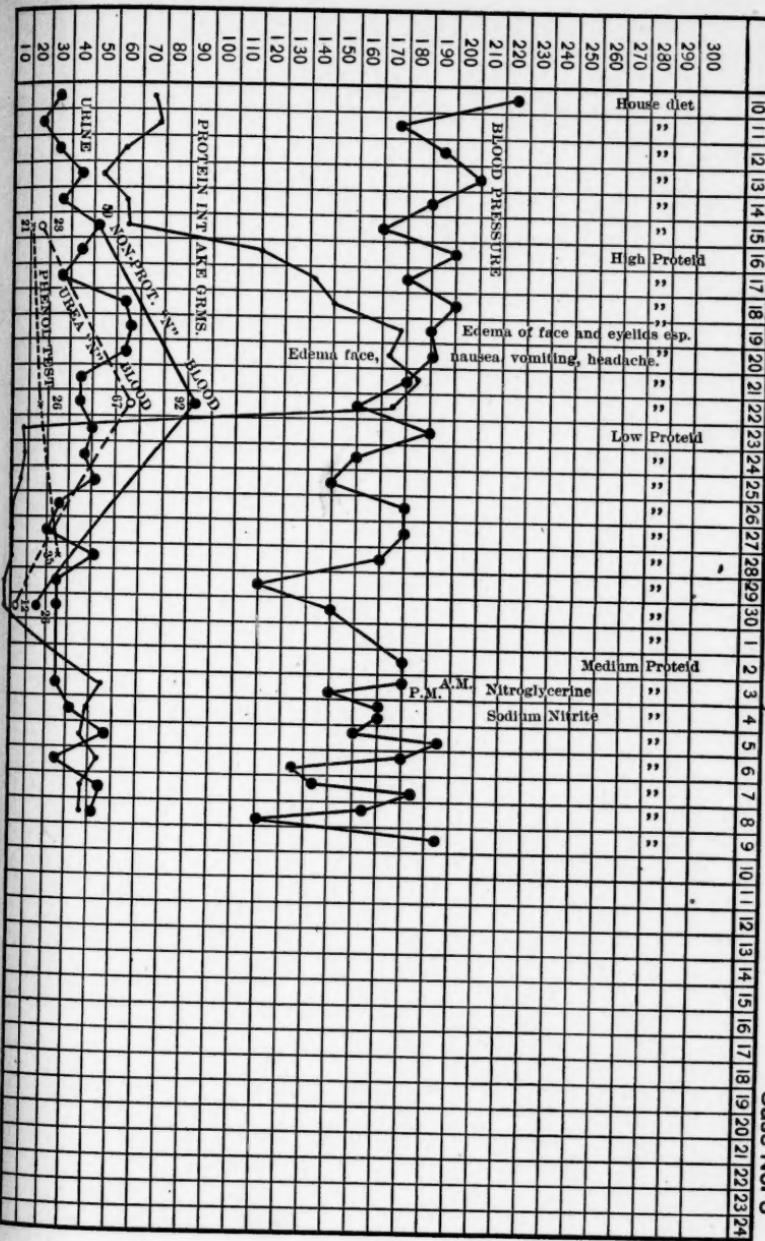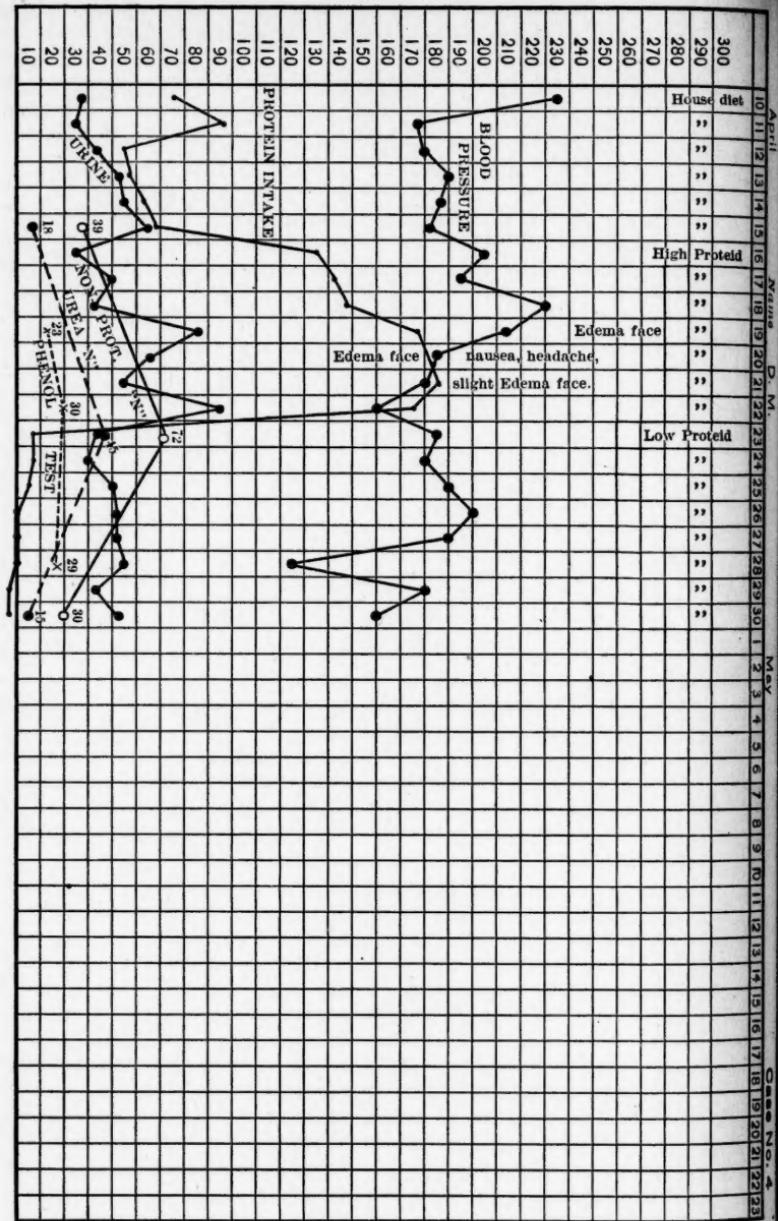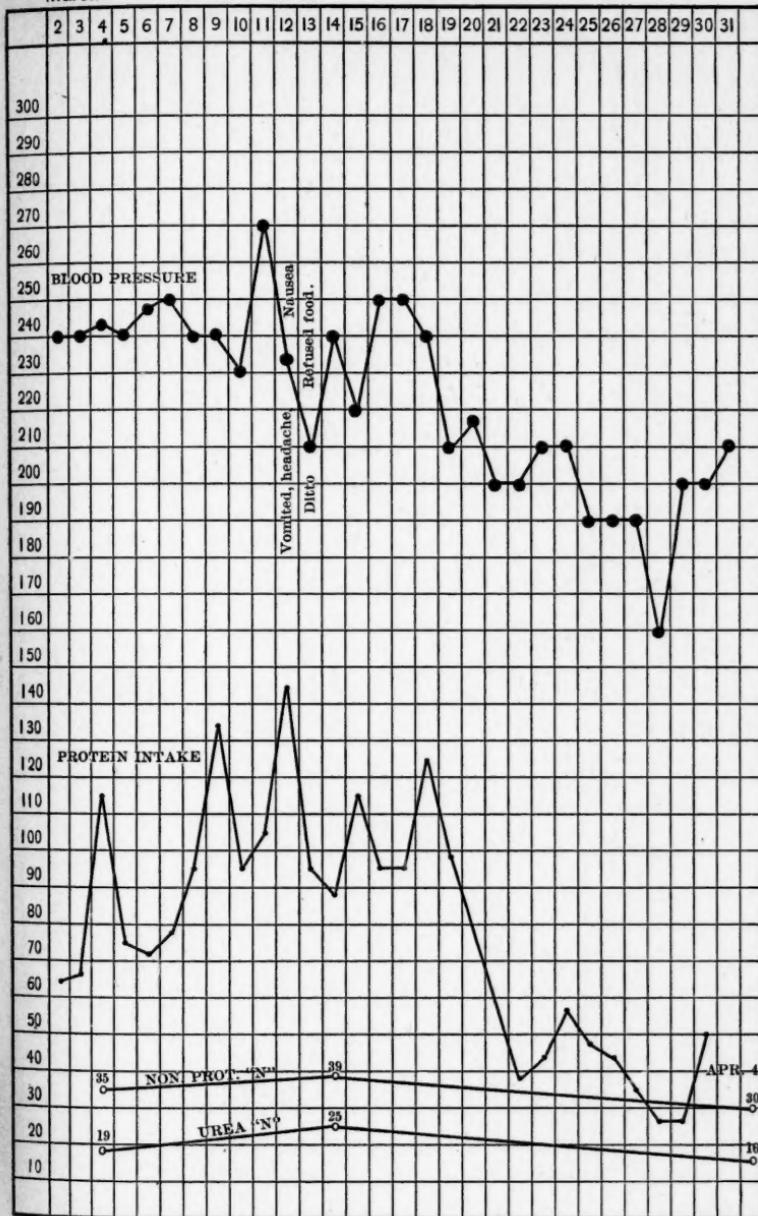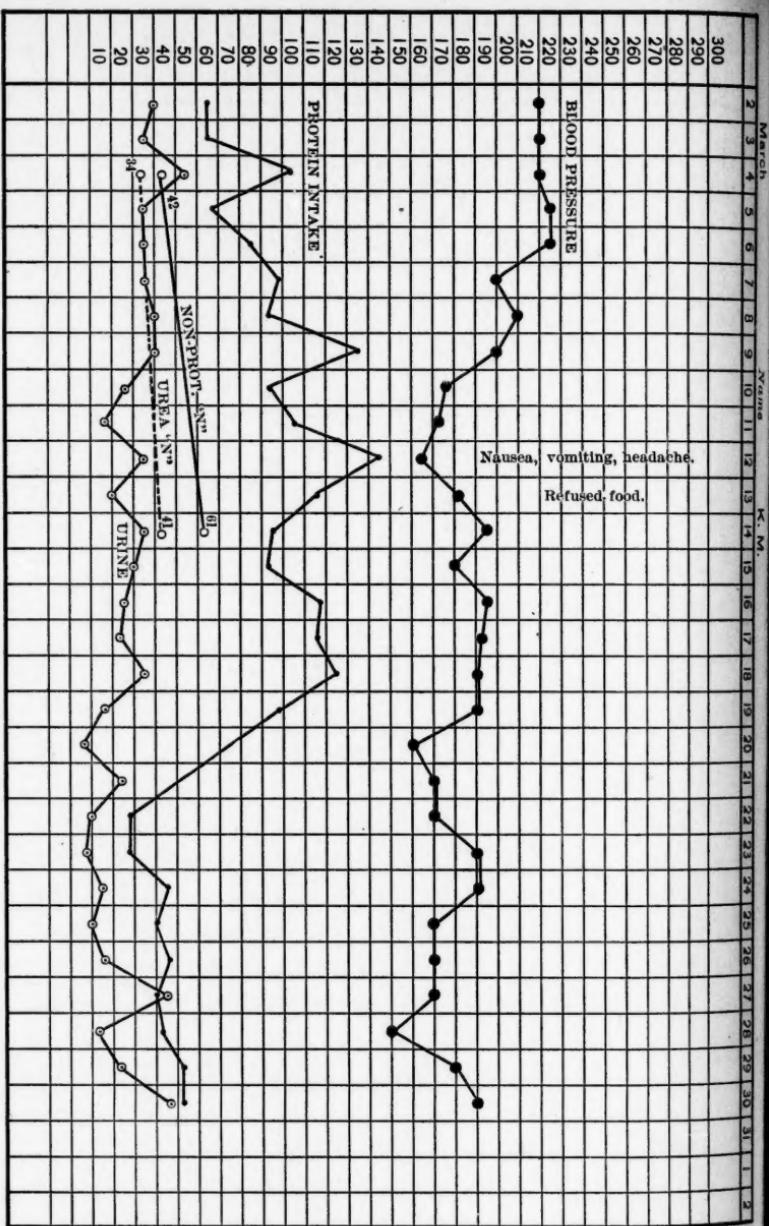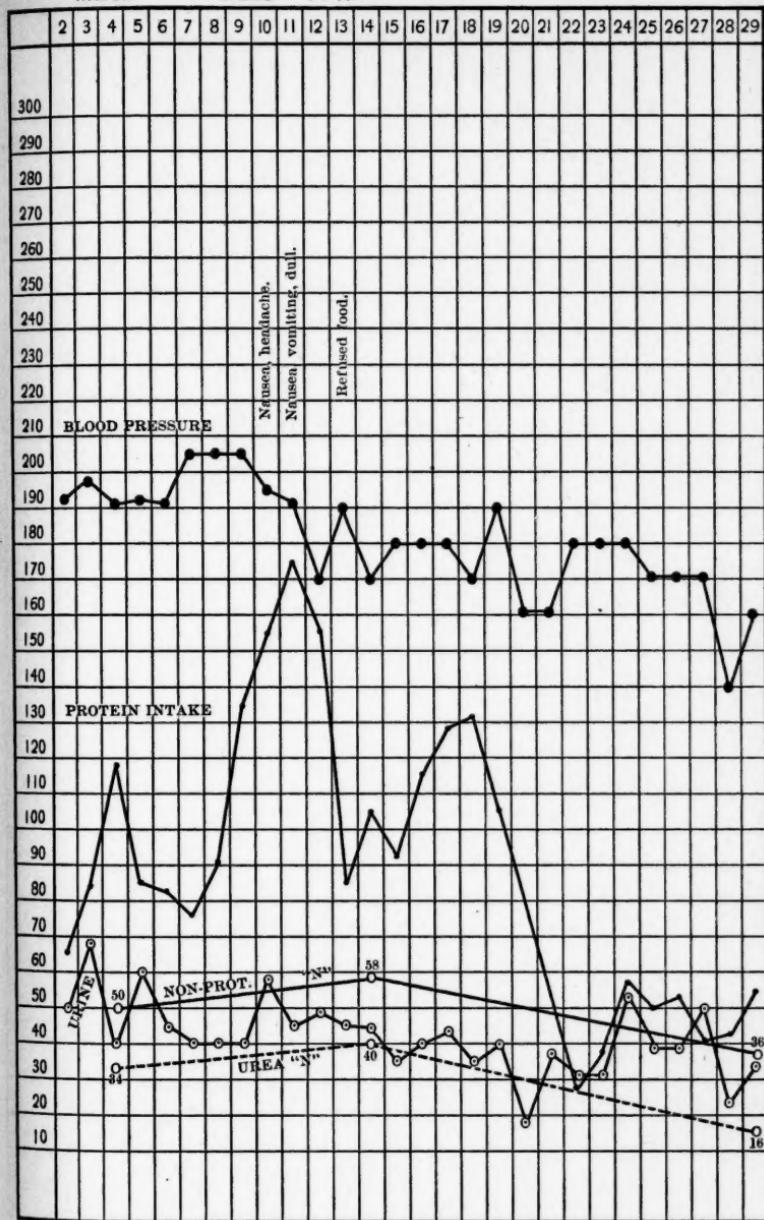
ARTICLE XIV.

GENERAL SUMMARY OF THE SIGNIFICANCE OF METHODS OF TESTING RENAL FUNCTION.

By Henry A. Christian, M.D.,
of Boston.

DELIVERED JUNE 10, 1913.

GENERAL SUMMARY OF THE SIGNIFICANCE
OF METHODS OF TESTING RENAL
FUNCTION.

In the preceding papers of the Symposium you have heard a discussion of the pathological types of nephritis and of the various methods used in testing renal function. Several of the speakers have described variations in renal function in individual cases as made out by different methods of testing renal function. It has been made evident to you that a number of new ways of inquiring into the activity of the kidneys have been provided which can be applied to patients reasonably easily. The question naturally arises, of what general value have these tests proved to be and how do they help in the management of patients having, or suspected of having, renal lesions?

In any case of renal disease, three problems present themselves to the physician or surgeon. (1) What is the actual condition in the kidney, or diagnosis? (2) What is to be the probable course and final result of the pathological condition, or prognosis? (3) What therapeutic measures should be applied in the management of the case, or treatment? Let us examine then briefly in how far these three problems are helped toward a solution by the newer methods of testing renal function.

DIAGNOSIS.

In the diagnosis of such renal lesions as are ordinarily treated by the physician we seek to know whether the kidneys are diseased or not, and if diseased, the nature of

the pathological process. In surgical conditions of the kidney these same problems present themselves and in addition the questions as to which kidney is the diseased one and whether the less diseased kidney is functionally capable of carrying on the excretory work of the body in the absence of the more diseased kidney become of .even greater importance. If by any of the various tests we can show that the kidney is not functioning in a normal way, we are justified in saying that the kidney is diseased. However, functional study of experimental lesions in animals has made it clear that a decrease in functional activity is not always accompanied by a demonstrable anatomical lesion, consequently we have to distinguish between a functional lesion and an anatomical lesion in the kidney. It is particularly in this field that functional tests have been useful. For example, it is their application at intervals which helps us to distinguish between a true nephritis and a renal disturbance consequent upon cardiac decompensation. In the stage of cardiac decompensation the kidney may show a marked functional disturbance in every way similar to that produced by a renal lesion of the nephritic type. In the former, however, with restoration of cardiac compensation as the result of appropriate therapeutic measures, the functional incapacity of the kidney disappears, while in the case of nephritis, though decreasing, disturbance of function of some nature remains to indicate an organic renal lesion.

In surgical conditions such as prostatic enlargement in a similar way repeated application of the functional tests serves to distinguish functional derangement consequent upon damming back of the urine from an actual diffuse renal lesion secondary to urinary stasis along with chronic infection. If the condition is merely the first, after a few days of permanent drainage the functional capacity is entirely or in great part restored, while in the second, no marked restoration of function takes place, indicating in

the first instance reasonable safety in operation, and in the second, increased risk, because anatomical changes in the kidney have reduced the excretory capacity of the organ to a point likely to prove insufficient for the needs of the body during the strain of operation and surgical convalescence. Where the problem is of the nature indicated by the examples cited, it is the phenolsulphonephthalein test which has proved most helpful. Here the excretion of coloring matter indicates quite well the total renal function and if the amount of the dye excreted is determined from time to time this aids much in diagnosing whether or not there is an actual diseased condition of the kidney.

In another type of case it is often important to know whether there is a nephritis with uremia present or not. This is particularly in patients who are in a condition of coma. It is often far from easy to determine whether a patient in coma is suffering from cerebral hemorrhage or from uremia. In each the urine may show albumin and casts. The determination of nitrogen retention in the blood by Folin's method or some other method should prove of very great value in just this type of diagnostic difficulty, and under these conditions would probably be of greater value than the phenolsulphonephthalein test.

The other methods of testing renal function, which depend upon selective excretory activity of different parts of the renal structure for various substances, while useful at times in making the diagnosis as to whether the kidney is diseased or not, should have greater value in determining the nature of the pathological lesion in the kidney, inasmuch as theoretically the rate of excretion of various substances ought to localize the lesion in glomerulus, tubule or blood vessel. Though this has been claimed by the advocates of these methods, an analysis of their results in cases which have been studied during life and examined at autopsy does not justify us at present in assuming that any very

accurate pathological diagnosis of the renal condition can be made on the basis of these tests. In other words, while the application of these several methods of testing renal function do help very greatly in diagnosing whether the kidney is diseased or not, they do not at the present time enable us to make an accurate diagnosis of the type of pathological lesion which we will find when the patient is subjected to post-mortem examination. The application of these methods, however, increases materially the probability of making a diagnosis during life which will harmonize with the findings of the pathologist, and in that sense methods for testing the function of the kidney have materially advanced our ability to diagnose renal lesions.

PROGNOSIS.

A patient presents himself who has some signs indicative of a lesion of the urinary tract amenable to surgical treatment. If operation is performed, is it likely that the renal function can be maintained under these conditions and the operation be successful in such a case? Here tests of renal function very often give data of greatest value in forming a prognosis. The prognosis at first seems bad, but preliminary treatment may cause a second test to become of better prognostic significance. Before preliminary treatment prognosis was bad and operation contraindicated; after appropriate treatment function may have greatly improved and operation become comparatively safe. The newer tests of renal function largely have furnished this information. In such a case the phenolsulphonephthalein test is particularly valuable in prognosis.

However, it must be kept clearly in mind that tests of renal function are not of very great aid in prognosis unless considered in relation to the general physical findings and the probable diagnosis. A very low phthalein output in a patient with prostatic obstruction indicates the need of de-

lay and preliminary treatment, which may convert a poor prognosis into a good prognosis. The same reduced phthalein output on the other hand in a case of chronic nephritis most likely would remain low and be of grave prognostic import.

The value of tests of renal function in prognosis of surgical conditions is now quite well recognized; their value in diffuse lesions, not capable of surgical treatment, is not so widely acknowledged. In the patient with nephritis the unsuspected, often very sudden, development of uremia, renders prognosis most difficult. Intimation of impending uremia is often given by the defective phthalein excretion and the nitrogen accumulation in the blood in these cases when symptoms and physical signs give no suggestion of uremia. It is in detecting early the approach of uremia that functional renal tests have been of greatest help in immediate prognosis. More remote prognosis in nephritis is aided much more by determining the ability of the kidney to excrete such substances as water, nitrogen, salt, lactose, etc. In all these cases it is not the single test made once that is of value, but the repetition of several tests.

Tests of renal function, however, may fail entirely to yield any prognostic information as to the factors which eventually kill the patient. Renal function may be relatively good, but cerebral hemorrhage or cardiac failure may develop and terminate the life of the patient with diseased kidneys. In all criticism of the prognostic value of any test of renal function cases of this type which prove fatal contrary to the indications of functional tests should not be regarded as failures in renal prognosis, rather as cases in which an event, not to be prognosticated from any form of study of renal function, has ensued with fatal result. If this possibility is kept in mind, a guarded prognosis will be given after tests of renal function, but yet a prognosis far more apt to tally with the prognosis of the disease than one

given without test of renal function. Other means than
tests of renal function should yield information as to the
probability of such incidents in the course of nephritis as
mentioned above and these combined with tests of renal
function will give data on which to base a reasonably cer-
tain prognosis.

TREATMENT.

Since intelligent treatment must be founded on a knowl-
edge of the diseased condition being dealt with, all
improvements in methods of diagnosis tend to improve treat-
ment. As already pointed out, tests of renal function have
helped materially in our ability to diagnose correctly renal
lesions. Consequently in this sense these tests have im-
proved our treatment of renal lesions.

Another important factor in successful treatment is our
ability to anticipate impending changes. Disturbances of
renal function that indicate the very early stages of a de-
veloping uremia put us in a position to begin a vigorous
eliminative treatment which often will avert the serious
forms of uremia or long postpone their development.

In the surgical treatment of renal lesions to know the
functional capacity of the kidneys and the probable prog-
nosis aids very greatly in selecting the proper operative pro-
cedure which will give to the patient the largest chance of
cure. This knowledge often will lead to operation in sepa-
rate steps which the patient can stand easily instead of a
single long operation apt to prove fatal. During surgical
treatment repeated tests of function are valuable aids in
determining procedure.

The effects of the different diets in cases of nephritis may
be expected to be measurable by the changes produced in
renal function, and these changes are indicated by varia-
tions in the results of functional tests. Up to now, how-
ever, too little investigation has been carried on along these
lines to justify any general conclusions as to the value of

the several tests.   Certainly, however, the output of water, salt and nitrogen are valuable guides in the determination of some factors in the diet for the nephritic.

Diuretic drugs need to be restudied by means of tests of renal function to enable us to decide what diuretics to use, when to push them and when to withhold them.   As with diet, too little is known to-day of diuretics from this point of view to make it worth your time to talk of them at any length.   It should be said, however, that present results from studies of this nature show that injury may be done the patient by the use of diuretics if their action on renal function is not studied at least by some of the simpler methods.

CONCLUSIONS.

Methods of testing renal function at present are of greatest value in determining prognosis; they help very much in diagnosis.   In treatment we are not in a position to evaluate them for relatively little work has been done on their relation to therapeutic measures.

Present methods of testing renal function have advanced very materially our knowledge of renal disease.   Most of these methods have been used relatively a short time and so we are not in a position to state which tests will prove of the greatest usefulness or how many and which tests should be applied in a single case.   No doubt better tests will be developed, but much remains to be learned about those already in use.   They have served to emphasize the functional conception of renal disease as compared with the structural, and this is a distinct advance.

As in all new fields of investigation it is likely that in the study of renal function enthusiasts will claim too much and critics will scoff.   A balance between the two views, however, must be taken to get an adequate appreciation of the value of tests of renal function.   In estimating this, it must be kept clearly in mind that tests of renal function furnish

given without test of renal function. Other means than tests of renal function should yield information as to the probability of such incidents in the course of nephritis as mentioned above and these combined with tests of renal function will give data on which to base a reasonably certain prognosis.

TREATMENT.

Since intelligent treatment must be founded on a knowledge of the diseased condition being dealt with, all improvements in methods of diagnosis tend to improve treatment. As already pointed out, tests of renal function have helped materially in our ability to diagnose correctly renal lesions. Consequently in this sense these tests have improved our treatment of renal lesions.

Another important factor in successful treatment is our ability to anticipate impending changes. Disturbances of renal function that indicate the very early stages of a developing uremia put us in a position to begin a vigorous eliminative treatment which often will avert the serious forms of uremia or long postpone their development.

In the surgical treatment of renal lesions to know the functional capacity of the kidneys and the probable prognosis aids very greatly in selecting the proper operative procedure which will give to the patient the largest chance of cure. This knowledge often will lead to operation in separate steps which the patient can stand easily instead of a single long operation apt to prove fatal. During surgical treatment repeated tests of function are valuable aids in determining procedure.

The effects of the different diets in cases of nephritis may be expected to be measurable by the changes produced in renal function, and these changes are indicated by variations in the results of functional tests. Up to now, however, too little investigation has been carried on along these lines to justify any general conclusions as to the value of

the several tests. Certainly, however, the output of water, salt and nitrogen are valuable guides in the determination of some factors in the diet for the nephritic.

Diuretic drugs need to be restudied by means of tests of renal function to enable us to decide what diuretics to use, when to push them and when to withhold them. As with diet, too little is known to-day of diuretics from this point of view to make it worth your time to talk of them at any length. It should be said, however, that present results from studies of this nature show that injury may be done the patient by the use of diuretics if their action on renal function is not studied at least by some of the simpler methods.

CONCLUSIONS.

Methods of testing renal function at present are of greatest value in determining prognosis; they help very much in diagnosis. In treatment we are not in a position to evaluate them for relatively little work has been done on their relation to therapeutic measures.

Present methods of testing renal function have advanced very materially our knowledge of renal disease. Most of these methods have been used relatively a short time and so we are not in a position to state which tests will prove of the greatest usefulness or how many and which tests should be applied in a single case. No doubt better tests will be developed, but much remains to be learned about those already in use. They have served to emphasize the functional conception of renal disease as compared with the structural, and this is a distinct advance.

As in all new fields of investigation it is likely that in the study of renal function enthusiasts will claim too much and critics will scoff. A balance between the two views, however, must be taken to get an adequate appreciation of the value of tests of renal function. In estimating this, it must be kept clearly in mind that tests of renal function furnish

but one set of facts about a patient, while for diagnosis, prognosis and treatment, clinical data from many sources are required, not the one test but the many are to be used if we reduce our clinical failures to their minimal number. Tests of renal function are of unquestioned value in renal disease, but they should supplement not supplant other ways of studying the nephritic.

Those who desire a more detailed statement of the value of tests of renal function are referred to the papers "On the Study of Renal Function," by Henry A. Christian, Theodore C. Janeway and Leonard G. Rowntree, presented at the meeting of the Congress of American Physicians and Surgeons, held in Washington, May 6, 1913, and published in their transactions; and to numerous studies which have appeared during the past two years in the medical journals.

AN ANATOMICAL AND SURGICAL STUDY OF PERICECAL MEMBRANES.

By Michael F. Fallon, M.D.,
of Worcester.

Delivered June 10, 1913.

AN ANATOMICAL AND SURGICAL STUDY
OF PERICECAL MEMBRANES.

WITHIN the past few years various operations have been undertaken for the relief of the frequently obscure syndrome of abdominal symptoms, pain, constipation, gas-distention, and intestinal autointoxication. Formerly, chronic appendicitis was generally held responsible for these symptoms, but since the results of operations for chronic appendicitis were frequently disappointing (30 per cent, Wilms[1]) to surgeons and patients alike because of the continuance of the symptoms, the discussion as to the etiology and operative measures have been directed to other conditions; among them the too restricted cecum (Jackson), and the too movable cecum (Wilms[2]). The disability in these two conditions is said to be due to pericecal and pericolonic membranes.

Although the so-called Jackson membrane and the *cæcum mobile* are different entities, they have this in common; that it is claimed for them that they, at times, cause a mechanical interference with the peristalsis of the first part of the large intestine with resulting stasis of its contents, and thus give rise to symptoms, chiefly pain, constipation, gas-disturbance and autointoxication. Surgical methods for the relief of these conditions is thus expressed by an advocate of them: "In such a case with the *cæcum mobile*, pericolonic membranes and kinked appendix, I, in some instances, remove the pericolonic membrane, remove the appendix, and fix the cecum and ascending colon well up in the flank."[3]

Jackson[4] describes his membrane as a "new adventitious, vascularized, investing layer of peritoneum covering the ascending colon."

Jackson,[4] Pilcher,[5] and others state that the membrane, when disabling, is due to inflammatory or infectious changes. originating within the intestine (colitis, stasis).

Flint,[6] as a result of investigations in both the fetus and adult, believes that the membrane is congenital, and may take its origin from the omentum, or, it may result from a dragging down of the peritoneum in the descent in the fetus of the cecum from its sub-hepatic position.

Blake[7] said that "the so-called Jackson membrane was always present, and was in fact a normal structure." The writer believes this statement of Blake to be true, and for the following reasons: He has always found this membrane when he has looked for it; it has all the characteristics of a normal, congenital, peritoneal membrane. It is a delicate structure of equal consistency throughout; even, transparent, and with orderly vascularization. It may be traced to the peritoneal plates of the omentum and may be seen to be continuous with them; especially, when an ascending mesocolon is present. But even when the ascending, colon is fused to the parietal peritoneum, the veil can be seen to be continuous with the serous covering of the mesocolon by detaching the fused parietal peritoneum. Here the veil may be seen running under the parietal peritoneum, and to be continuous with the mesocolon. The same membrane envelopes the remaining colon having the same characteristics that it has on the ascending colon. This may well be seen on the transverse colon.

Gray[8] says, "The mesentery is seen to be formed of two layers of peritoneum, which surround an intestine completely, except at a posterior line where there is opportunity for vessels, nerves, and lymphatics to enter or return. Two layers of peritoneal connective tissue, which lodge vessels, nerves and lymphatics, constitute a mesentery. The intestine looks as though it had pushed its way into the sac of peritoneum as a finger enters a glove. That comparison

is incorrect, for intestine and peritoneum are developed simultaneously."

Hence, the writer believes that the Jackson membrane is a congenital, normal, constant structure, and is not disabling to the cecum and ascending colon, and is not a membranous pericolitis. That there is a definite pericolitis, however, is established. But the pericolitis to be described, has no relation whatever to the so-called Jackson membrane.

In 1910 [9] the writer reported a case of pericolitis as follows:

Pericolitis is a patch of isolated, circumscribed, adhesive peritonitis on the outer wall of the colon, and occurs especially at the site of the *flexura coli dextra* or *sinistra*, or on the sigmoid (Virchow [10]).

Historically, it is of interest, inasmuch as it was first described by Virchow, who gave a clear, pathological description of it. He said he found it often, and while he could not speak definitely of its clinical manifestations, he believed that many cases of pericolitis were falsely diagnosed as inflammations of the gall bladder or similar diseases. He ascribed the cause of it mostly to fecal stasis.

The disease and Virchow's description of it were forgotten for almost forty years, until surgical abdominal exploration revealed a number of cases, and these were reported between the years of 1890 and 1900. The entity of the disease became the subject of frequent discussion in German medical literature: some men, e.g., Leube, Windscheid, Bittorf, et al., claiming that it was an independent affection, while others, e.g. Nothnagel, were skeptical as to its occurrence.

Authentic reports from pathologists, surgeons and internists, however, have been so numerous, that no one, I believe, now doubts the occurrence of pericolitis as an independent disease, and the pathological description of it by Virchow over half a century ago, has never been excelled either in accuracy or in completeness. It is important at

times to bear in mind the possibility of this affection since it may simulate various other abdominal diseases, e.g., appendicitis, disease of the gall bladder or cancer of the stomach, etc.

Its symptoms are those which one would expect from an isolated, circumscribed patch of peritonitis, e.g., localized pain, tenderness, abdominal wall rigidity. The severity of the symptoms naturally depends upon the severity of the lesion, e.g., it may be mild and evanescent, or exceptionally, it may be so severe as to cause a diffuse, suppurative fatal peritonitis. The illness may last but a short time — a few days, or it may continue for weeks or months, during which time there may be apparent improvement and relapses. Improvement may and generally does follow without operation. In one of our cases the affection was acute, in the other chronic. A brief description of the latter follows: The patient, a married woman, 42 years old, had, previous to her entrance into the hospital, complained of pain in the right side of the abdomen. Of late the pain was continuous, and it frequently kept her awake all night. The pain was sharp, not crampy; it did not go to the back, and was not dependent on eating. She was at no time confined to the bed, nor was she at any time completely incapacitated by reason of it. She had suffered from obstinate constipation for years.

Examination showed tenderness, and abdominal wall rigidity on pressure in an area the size of the palm of an adult hand, midway between McBurney's point and the right costal margin, nipple line. A diagnosis of high appendix was made. Operation, however, showed nothing wrong with the appendix, or with the gall bladder. The right (hepatic) flexure of the colon, and its omentum, were adherent to the anterior parietal peritoneum over an area the size of the palm of an adult hand. These were freed. The wall of the colon was very much thickened; its serosa abnormally injected and uneven. The other abdominal organs were apparently nor-

mal: no other adhesions were found. A piece of the affected
tissue was excised for pathological diagnosis, and the pathol-
ogist reported: *   "Chronic inflammation throughout con-
nective tissue; surface infiltrated with lymphocytes; one
end necrotic with foci of lymphocytic infiltration. Chronic
inflammation." The patient left the hospital free from her
former symptoms, and two months afterward said that she
did not have a return of them.

CÆCUM MOBILE.

Wilms [11] claims that a too-movable cecum at times may
interfere with peristalsis, and thus cause constipation and
pain, — traction-pain. He claims that by cecopexy (fixation
of the cecum and ascending colon to the retroperitoneum)
the majority of his patients are cured.

The movable cecum is due to the presence of an ascending
mesocolon.

Treves [12] says, "A meso-colon may be expected on the left
side in 36 per cent of all cases, on the right side in 26 per
cent." Dreyer [13] says that 67 per cent of autopsies that he
had made had a movable cecum, and that it was hardly pos-
sible that this condition was pathological and a primary
cause of obstruction. The writer examined one hundred
subjects in the Harvard Medical School and found an ascend-
ing meso-colon in twenty-four of them.

The transverse colon always has a mesentery, at times so
long that the transverse colon is in the pelvis. The mesen-
tery of the sigmoid flexure is so long that the ancients de-
scribed the normal position of the sigmoid to be on the right
side of the body.[14] Hence the transverse colon and sigmoid
flexure always have a mesentery, and the ascending and
descending colon have it so frequently that its presence
instead of the fused colon should be regarded as the less
common form of attachment rather than as pathological.

* Path. Diag. (Harv. Med. School), No. 10667.

From a clinical and surgical standpoint it is profitable to consider the evidence of the surgeons in the German Surgical Congress of 1911, when Wilms read a paper on "Cæcum Mobile." The majority of the surgeons who took part in the discussion, opposed the views of Wilms more or less.[15] Notably, Sonnenburg, who claimed that the movable cecum in itself was not pathological — that there was not sufficient reason for making a clinical entity of the movable cecum, and that a diagnosis of this condition may be made when in reality colitis is present, and that the x-ray diagnosis is not trustworthy.

There is an apparent contradiction in the operative measures applied to Jackson's membrane and to the mobile cecum.

The respective advocates of these conditions claim that the mechanical disability in the one case is due to the too limited movements of the intestines, while in the latter case, it is due to the too free movements. Wilms advises the binding down of the intestine while Jackson advocates the loosening up of the intestine.

William J. Mayo [16] sums up the results of operations in these cases as follows:

"That many of the patients operated on have been greatly benefited cannot be denied, yet if one were to take the case histories and reports of successful treatment by means of such mechanical therapy and put them all in a hat to be picked out at random, one could not determine from the histories of the patients those who had been relieved of symptoms by operating for mobile cecum, for relief of the adhesions, for mobility of the sigmoid, for fixation of the sigmoid, for prolapse of the stomach, and, for that matter, for movable kidney. The histories read alike, but the operations seem to vary with the bias of the operator. Are all of these deductions wrong? Have the profession in regular medicine with their accurate observations no conclusions which depend upon more authentic data? To say that relief

of symptoms demonstrates the truth of the opinion is not sufficient unless we grant the same privilege to the mental healers."

There is a great deal of confusion in the various theories as to the cecum and the surrounding membranes being the source of constipation and pain, and in some of these theories a very important physiological fact may be lost sight of, i.e., that digestion in man requires the retarding of the food current in the ascending colon. The accumulation in the beginning of the large intestine in itself is not pathological. Sonnenburg,[11] Huntington [17] and Cannon [18] have shown that many of the features of the large intestine instead of being a menace to the well-being of man (Metchnikoff, Lane) are on the contrary most admirably adapted to the completion of his digestion. Food in transit from the stomach to the anus usually requires from 24 to 36 hours, only 6 to 8 of which are occupied by the small, and the remainder by the large intestine.[19] Most of the nutriment is absorbed in the small intestine, but about 50 per cent of the fluids and 10 per cent of the solids are absorbed in the first half of the large intestine (Mayo [16]); and here necessarily, because of the character of the nutriment, a longer time is necessary for absorption. Even the anatomical up-hill arrangement of the ascending and transverse colon serves a physiological purpose.

"The splenic flexure of the colon is held high as a mechanical means of maintaining food products as long as possible in the first half of the large intestine. This method of retention is more economic in its operation than a muscular sphincter apparatus would be." (Mayo [16].)

"Even when the cecum is of moderate size or rudimentary, as in the cat, prolonged retention of the material delivered by the small intestine is provided for in the reversed peristalsis which prevails in the proximal colon." (Cannon [18].)

"Food rich in cellulose may remain in this region (the

cecum) for days undergoing changes which result in its being utilized in the body." (Cannon [18].)

"On the other hand, in carnivorous animals, digestion occurs principally in the stomach and small intestine; the cecum is either rudimentary or absent." (Cannon [18].)

Therefore, the construction of the large intestine in man with its accessory modifications (Huntington [17]) favors the retarding of the food current in its first portion for physiological purposes; and when this retarding amounts to a pathological stasis, with its accompanying symptoms, of pain and constipation, the causes may be sought for elsewhere, and frequently may be traced to faulty habits and neglect of physiological laws. It is a noteworthy fact that this pathological stasis obtains mostly in women: (75%, Wilms [1]), and is frequently associated with gastro-coloptosis. (Rovsing [20].)

Hence, for the present at least, obstinate constipation and its concurrent symptoms, as a rule, should be treated by hygienic, dietary and therapeutic measures. Exceptionally, perhaps, surgery may be necessary, but extreme care should be used not alone in selecting suitable cases for operation, but also in the applying of logical operative measures, lest mutilation rather than amelioration ensue.

RELATION OF PERICECAL MEMBRANES TO APPENDICITIS.

Professor Albrecht's work [21] on the relation of pericecal membranes to appendicitis is authoritative and founded on fact. His investigations were made on the cadavers of 500 children under six years of age. He found to his astonishment that 15 per cent of these subjects showed malpositions and deformities (kinks and twists) of the appendix, due to these membranes and that these anomalous positions gave opportunity for interference with drainage, and the possibility of future appendicitis. The opportunity for entanglement of the appendix is given by the long distance that the cecum

has to travel in its fetal excursion before it finally reaches its permanent position.

The appendix, as a result of these adhesions, may lie on the anterior surface of the kidney, even as high as the upper pole; it may adjoin the under surface of the liver, or may lie on the descending portion of the duodenum or on the fundus of the cecum; it may be attached to the ileum, or may be buried in the pericecal fossæ; it may be covered in whole or in part by the membranes.

Albrecht says that he has not been able to find the retroperitoneal appendix. The appendix may often seem to be retroperitoneal, but, in reality, it is surrounded by the peritoneum and the enveloping peritoneal membrane may bridge over the appendix from peritoneum to peritoneum, and either surrounds the appendix, or has peritoneum underlying it. Surgeons generally corroborate the findings of Albrecht, i.e., that interference with drainage is the most common cause of appendicitis. Dieulafoy [22] said, that appendicitis is always the result of the transformation of the canal of the appendix into a closed cavity. Aschoff [22] "without stagnation, no appendicitis." Tyrode [23] says, "when there is inflammation and excessive secretions in the intestine, these may easily pass along, but if the same condition exists in a kinked or constricted appendix, much more severe pressure and inflammation takes place, which may result in an acute or subacute attack of appendicitis." And again, "we feel very little confidence in the recent articles on the hematogenous origin of appendix inflammation." Since, then, congenital pericecal membranes may predispose to appendicitis, "there can be no doubt that such congenital anomalies are hereditary, and consequently may run in families." [21]

In 1910, the writer, as a result of investigations as to family appendicitis, reported that 24 out of 200 patients operated by him for appendicitis were members of families

in which one or more members had previously been operated for appendicitis.

A striking example of this family type occurred in the writer's practice during the past year. The patient, a young man, was operated for acute appendicitis. Six members of his family, five brothers, two of whom were physicians, and one sister, had previously been operated for appendicitis. Three of them were operated by Dr. Bottomley. The ages of all at the time of operation were between twenty and thirty. The only remaining member of the family, a sister, has chronic appendicitis. An uncle had peritonitis, resulting from appendicitis. The grandmother died of appendicitis.

Conclusions. The so-called "Jackson Membrane" is a congenital, normal, peritoneal membrane and is not a membranous pericolitis.

It may be confused with the pericolitis of Virchow.

The ascending mesocolon is a less frequent form of attachment of the ascending colon: and the accompanying *Cæcum Mobile* in itself is not pathological.

Digestion in man requires the retarding of the food current in the first half of the large intestine — the physiological stasis. When this stasis is pathological, the causes frequently are faulty habits, and hygienic and dietary, rather than surgical measures, as a rule, are indicated.

Pericecal membranes frequently predispose to appendicitis, and afford one explanation for family appendicitis.

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DISCUSSION OF ARTICLE XV.

DR. J. C. HUBBARD, Boston: After learning from an abstract the contents of Dr. Fallon's paper I had prepared a discussion but I think these remarks are not worth making now, as it seems to me that Dr. Fallon has covered the subject admirably. I think he has given the proper values to the various membranes, and it seems to me it would be a waste of time to say anything more except to congratulate him upon his paper.

DR. S. A. MAHONEY, Holyoke: The paper of Dr. Fallon has been very illuminating and instructive to me. However, I believe that the entire medical profession will not indorse unqualifiedly, his conclusions, as all are not in harmony on this subject.

I had the pleasure, last month, of attending a meeting in New York, at which I heard Mr. E. G. Schleisinger, who is associated with Mr. Lane in his work at Guy's Hospital.

The subject of discussion was "the membranes in the right iliac fossa." He differs from the writer, in that any of these membranes in that locality are inflammatory. He agrees with the writer in saying that the majority of the membranes down there are entirely physiological. They come into the hands of the surgeon only when they are developed to a pathological degree. He likened them to guy ropes, holding a hollow, overloaded tube from sliding down into the true pelvis. In that they are physiological. When, however, the patient is not successful in passing the intestinal contents, and there is a stasis of these contents, you get symptoms of autointoxication. All these membranes, Mr. Schleisinger maintained, in the beginning are physiological, and, as I say, it is only when they are developed greatly, interfering with the peristalsis, that they become pathological. In the discussion, relative to whether these membranes were inflammatory or non-inflammatory, Mr. Schleisinger said that they were entirely physiological, and non-inflammatory, from the fact that in the beginning all these membranes were avascular. While on the contrary, if they were inflammatory membranes, in the beginning, they would be vascular, later becoming non-vascular.

Not only that, but he claimed that these membranes were always attached to the intestines, opposite the mesentery, and then around the bowel onto the lateral peritoneal wall, fan-shaped.

Mr. Lane has had opportunities for observing these membranes from the time of their very beginning, until they are thick. Always at the beginning they were avascular membranes. The blood vessels never came through the walls of the intestines, but from the lateral peritoneal wall.

He said that a very curious thing was this, that he had never noticed this condition in red-haired persons. He cited an example, in which there was a beautiful "Titian-haired" woman, who came to him for an operation for a Lane kink. At the operation, one of the attendants remarked that it was against his teachings to find this in a red-haired person. At the termination of the operation, he stripped the clothing down, and the pubic hair was black, thus proving his contention that red-haired people are less subject to these conditions than dark-haired.

It is claimed that the pathological part of this could be avoided in ninety per cent of the cases. That those cases that become surgical, usually become so in consequence either of neglect on the part of the owner of the membranes, or in consequence of poor medical treatment at the beginning. That ninety per cent are perfectly curable by well advised medical treatment, and only about ten per cent finally come to the surgeon.

DR. F. B. LUND, Boston: I think this is a very important and interesting subject. It seems to me that we are not so much interested in how these connections develop, as in what they do to our patients when they are there. The fecal current in the large intestine is slow, and it has to be slow on account of the consistency of the intestinal contents; but it has been my experience in a good many operations for intestinal adhesions, that all sorts of adhesions may bind up the small intestine without obstructing it, while almost any bands across the colon cause serious colic and constipation and the general symptoms due to intestinal stasis. Adhesions of the sigmoid flexure to the abdominal wall have caused persistent constipation in patients whom I have been called upon to treat. These cases may be cured sometimes by the simple procedure of removing the band and sewing it together in the opposite direction; sometimes, a short-circuiting operation has been of help in cases where previous attempts at dividing adhesions have been ineffective.

I operated yesterday upon a patient who had had the appendix and gall-bladder operated upon and had obstruction. X-ray showed things coming to a definite end right at the hepatic flexure of the colon. He had lost about forty pounds; examination showed old adhesions, mostly inflammatory, extending across the colon, binding it down and kinking it.

Each of these cases must be treated according to the actual conditions found in it. The symptoms must be very carefully worked out. The surgery should be done by those who have devoted a good deal of attention to this field. It is a difficult field but there is occasionally a brilliant success.

ARTICLE XVI.

RELATIONSHIP BETWEEN GYNECOLOGICAL AND NEUROLOGICAL DISEASES.

By W. P. Graves, M.D.,
of Boston.

Delivered June 10, 1913.

RELATIONSHIP BETWEEN GYNECOLOGICAL AND NEUROLOGICAL DISEASES.

An intimate relationship between the female genital organs and the nervous system has been recognized from the earliest times. Hippocrates regarded the uterus as the starting point of most nervous manifestations, and named from it one of the commonest of nervous diseases. This ancient idea was held with little modification up to comparatively recent times. In the middle of the last century such well known writers as Scanzoni, Amann, Romberg and Leubuscher, described hysteria as a "reflex neurosis resulting from genital irritation," and agreed that "every pathological change of the uterus, ovaries and tubes may be the precursor of hysteria." Even at the present time the celebrated Italian gynecologist, Bossi, is advocating by a prolific amount of literature the theory that minor gynecological lesions are the direct underlying cause of serious nervous and mental conditions.

An exaggerated conception of a direct relationship between pelvic abnormalities and nervous disease has led in the past to grave errors and has been the means of casting much discredit on the science of gynecological surgery. In the earlier days operations for lacerated cervix and later, ventral suspensions of the uterus, castrations, nephropexies, resections of cystic ovaries have been done by the thousands for the relief of nervous symptoms without sufficient surgical indication. In most recent times the same tendency has been seen in the excitement over autointoxication, enteroptosis, Lane's kinks and Jackson's membrane's, etc., in which the relationship between abdominal aberrations and nervous manifestations has been often greatly exaggerated and many

useless operations have been done. On the other hand the neurologists alarmed by this *furor operandi*, and impressed by the numerous surgical failures, have also erred and attempted to cure by long-drawn-out psycho-therapeutic treatment, cases which in reality require surgery. In other words, there has been too little team work between the surgeon and the neurologist and it is the object of this paper partly to emphasize this fact and partly to make certain suggestions by which we may come to a truer understanding of that difficult class of patients which requires both gynecological and neurological treatment.

INFLUENCE OF MENSTRUATION ON THE NERVOUS SYSTEM.

In considering the relationship between the genital and nervous systems one naturally regards first the important influence which the function of menstruation has on the general organism of a woman.

John Goodman in 1878 in an essay entitled "The Cyclical Theory of Menstruation"(Amer. Jour. Obstet.) was one of the first to call attention to the fact that the function of menstruation is not a purely local process but the expression of a profound change in the general circulatory system. This periodic change in the circulation Goodman regarded as under the direction of the nervous system and as following a regular law of rhythmic rest and activity such as is represented by the heart action.

Mary Putnam Jacobi in the Boylston prize essay of Harvard University for 1876 presented under the modest title of "The Question of Rest for Women during Menstruation" a most valuable contribution to the physiology of the pelvic organs, by expounding for the first time the *wave* theory of menstruation.

According to this theory, menstrual blood represents the overflow of superfluous nourishment material which has been stored up as a provision for impregnation, but which when

impregnation does not take place is discharged in the form
of a catamenial flow.

Jacobi saw in this a rhythmic wave in the metabolic proc-
esses of woman which reaches its maximum immediately
before and its minimum immediately after menstruation.
In order to prove her theory Jacobi made monthly observa-
tions on several women and established that just before the
menstrual period there is an increase in the body temperature,
in the blood pressure, in muscle strength and in the pulse
beat, all of which gradually diminish during the menstrual
period and are at their lowest ebb at its close.

These observations were confirmed by other investigators.
In 1890 von Ott and his pupil Schichareff (Zentralbh. f. Gyn.
1890) studied in 57 normal women through 68 menstrual
periods the temperature, pulse, blood pressure, muscle
strength, lung capacity, inspiration and expiration strength
and the ocular reflexes, and from these studies concluded
that the energy of the functions of the female organism is
at its height immediately before menstruation and that it
diminishes from the time of the beginning of the flow of
blood. Von Ott constructed a curve which represents graph-
ically the monthly wave of the life processes of normal woman
(Zentr. f. Gyn. 1910).

The discussion as to the physiological cause of this men-
strual wave of depression, whether it is the result of an ovarian
internal secretion, whether it is from a rhythmic change in
the central nervous system, or what not, does not at present
concern us. The curve of Ott shows plainly that there is in
the organism of the healthiest women a monthly period of
depression in her vital processes which finds definite expres-
sion in all her activities. This fact is of the very greatest im-
portance in our understanding of a woman, either as an
individual or as a patient. As Havelock Ellis (Man and
Woman) has pointed out the blood pressure chart of von Ott
would probably be paralleled, if it were possible to make

accurate observations, in all the senses, emotions and intellectual activities of women.   In fact, such a series of tests has been made of the eye by Finkelstein of St. Petersburg.

> " Finkelstein studied the functional activity of the eye during menstruation in twenty healthy women, aged between nineteen and thirty-three.   He found that during the period there is a concentric narrowing of the field of vision, beginning one, two, or three days beforehand, reaching the greatest intensity on the third or fourth day of menstruation, and gradually disappearing on the seventh or eighth day after its appearance. The narrowing is more pronounced in those women in whom menstruation is associated with malaise, headache, cardiac palpitation, and other nervous symptoms, as well as in those who lose large quantities of blood. Not only the field of vision for white but also the visual fields for green, red, yellow, and blue undergo a regular diminution.   Perversion of perception of green (which is seen as yellow) is observed fairly often (in 20 per cent cases).   Central vision is but slightly impaired, and rapidly returns to the normal standard after the period, and refraction remains intact."

There are numerous changes at the menstrual epoch that are more familiar.   There is a feeling of tension in the pelvis; the breasts often enlarge and become tense and painful; the thyroid gland becomes congested; the peripheral blood vessels of the skin often become flushed; while in brunettes, the pigmented areas around the nipples become deeper in color and dark rings may appear under the eyes.   I have one patient in whom large ecchymotic areas appear periodically on the thighs and legs during the menstrual period.   It is a well-known fact that the voice is affected during menstruation and in some places on the Continent provision is made that opera singers shall not perform during that period.

On the psychic and nervous side of perfectly healthy women the menstrual curve is still more plainly demonstrated.   There

is at that time a greater sensitiveness and impressionability. The individual is far more irritable and subject to outbursts of ill-temper and to unreasonable caprices. There is markedly less self-control and an invariable tendency to depression. The nervous reflexes are impaired and women are less skillful and dextrous during the menstrual period.

What we have said so far relates to women in perfect health. Under pathological conditions the same upward and downward curve occurs, but the changes may become much exaggerated.

In considering the pathological aspects of the relationship between menstruation and nervous disorders we must view the subject from two standpoints. First, the condition where abnormal menstruating function produces psychoneuroses in an individual otherwise sound as to her nervous system and, Second, the case where an abnormal condition of the nervous system is greatly aggravated or makes its only appearance during the menstrual period.

NEUROSES AS A RESULT OF MENSTRUAL IRREGULARITIES.

Of the menstrual irregularities that may produce neuroses, dysmenorrhea is by far the most important. By the term dysmenorrhea I refer to the so-called essential dysmenorrhea which consists of cramplike pains of the uterus felt usually in the front of the lower abdomen, occasionally in the sacral region. The pains of pelvic inflammation, chronic appendicitis, or other abdominal disease that are exaggerated during menstruation are not included under the term essential dysmenorrhea. Essential dysmenorrhea is undoubtedly a purely physical sign and in the majority of cases has some definite anatomical basis. The condition commonly associated with true dysmenorrhea is a local hypoplasia of the genital organs in which there usually exists a malposition of the uterus, in the form of a retrocessed anteflexion or a

retroversion-flexion of developmental origin, or there may be malposition without hypoplasia. In a great number of these cases the individual is otherwise perfectly normal and there is often no predisposition to lack of nervous equilibrium. The painful periods at first often have little effect on the patient; but gradually as she grows from girlhood into womanhood permanent nervous manifestations of irritability, exhaustion, and depression make their appearance. The curve of menstrual depression becomes deeper and deeper and the return to the normal becomes later and later during the intermenstrual period. Such patients no sooner recover from the effects of one period than they begin to dread the effects of the next one. The condition is therefore one of continual hammering at the patient's nervous system and eventuates gradually in seriously affecting it. It is no wonder, therefore, that patients with dysmenorrhea always in time become neurotic. The mistake, however, must not be made in supposing that the dysmenorrhea is in these cases the result of the neurotic condition. It is held by some that psychic and nervous conditions may induce chronic dysmenorrhea. This may be true in some instances; but in my experience it is so uncommon as not to be regarded seriously in the routine treatment of the cases under discussion. These cases are, therefore, primarily for the gynecologist who must do what he can to relieve the underlying condition. Unfortunately essential dysmenorrhea is difficult to treat successfully, but a certain percentage, (50-65%), yield to surgical treatment with immediate improvement of the nerous condition.   It sometimes happens that the dysmenorrhea cannot be cured by any known means and the patient develops into a hopeless invalid, a burden to herself and her friends.   In these extreme cases castration with hysterectomy is justifiable and indicated.   In properly selected cases the cure of the mental and nervous condition may be complete.

If neuroses persist after relieving the dysmenorrhea the patient becomes a subject for neurological treatment for then the symptoms in the absence of other physical causes are due to a congenital neurotic predisposition or else they are an expression of the so-called habit neuroses, a subject which will be referred to later.

Other irregularities of menstruation besides dysmenorrhea may be the underlying cause of psychoneurotic conditions. Menorrhagia, for example, may so deplete the patient's general health and resisting power as to produce neurasthenic states, especially if there be coupled with it the fear of cancer. Continued amenorrhea may be the cause of mental depression; but where it is associated with grave mental disorders such, for example, as dementia precox, it must be regarded only as a symptom of the disease.

It should be remarked at this point that disturbed psychic states may exert a certain amount of influence over the function of menstruation. It is extremely common for gynecological patients who are being prepared for operation to menstruate much out of their regular time. Sudden nervous or physical shocks often bring on the menstrual flow. It is doubtful if ordinary nervous shocks cause permanent irregularity though this claim is frequently heard in medico-legal cases. Fear or nervous shock may also cause temporary amenorrhea, as is often seen in women who fear impregnation, the menstrual period sometimes being delayed as much as ten days or two weeks under the influence of such apprehension.

INFLUENCE OF MENSTRUATION ON PATHOLOGICAL MENTAL AND NERVOUS CONDITIONS.

In this class of cases the primary seat of trouble is in the nervous system itself and it includes everything from hereditary functional disorders to serious organic mental disease. There is no doubt that all of these conditions are

aggravated during the menstrual period. If in addition, the menses are also abnormal, the reaction on the nervous system is greatly increased.

The nervous disturbance may be expressed only by severe periodic headaches. Hysteria, hysteroepilepsy, epilepsy, erotomania, dipsomania, kleptomania, and melancholia frequently appear chiefly or solely at the menstrual period. Women with criminal or suicidal tendencies often show their inclinations at that time. To quote again from Havelock Ellis:

> "Lombroso found that out of 80 women arrested for opposition to the police, or for assault, only nine were not at the menstrual period. Legrand du Saulle found that out of 56 women detected in theft at shops in Paris, 35 were menstruating. There is no doubt, whatever, that suicide in women is specially liable to take place at this period; Krugelstein stated that in all cases (107) of suicide in women he had met with, the act was committed during this period, and although this cannot be accepted as a general rule (especially when we bear in mind the frequency of suicide in old age), Esquirol, Brierre, de Boismont, Coste, Moreau de Tours, R. Barnes, and many others have noted the frequency of the suicidal tendency at this period. In England Wynn Westcott has stated that in his experience as a coroner, of 200 women who committed suicide, the majority were either at the change of life or menstruating; and in Germany Heller ascertained by post-mortem examination of 70 women who had committed suicide that 25 (or in the proportion of 35 per cent) were menstruating, a considerable proportion of the remainder being pregnant or in the puerperal condition.

. . . .

> "Among the insane, finally, the fact is universally recognized that during the monthly period the insane impulse becomes more marked, if, indeed, it may not appear only at that period. 'The melancholies are more depressed,' as Clouston puts it, 'the maniacal more

restless, the delusional more under the influence of their delusions in their conduct; those subject to hallucinations have them more intensely, the impulsive cases are more uncontrollable, the cases of stupor more stupid, and the demented tend to be excited.' These facts of morbid psychology are very significant; they emphasize the fact that even in the healthiest woman a worm, however harmless and unperceived, gnaws periodically at the roots of life."

The preceding cases are primarily for the neurologist and the psychiatrist, yet there are certain of them whom the gynecologist may relieve. Cases of dysmenorrhea or menorrhagia should be submitted to the gynecologist, for if these symptoms can be cured the patient is relieved of an important nervous irritant. A limited number of cases of this class where the manifestations appear solely at the catamenial period are subjects for castration as I have at different times shown in some of my own cases.

FUNCTIONAL NEUROSES ASSOCIATED WITH GYNECOLOGICAL DISEASE.

Under this heading we are dealing with a problem quite similar to that under the heading of menstruation excepting that the genital irritation of the nervous system is exerted not periodically but continuously as the result of chronic pelvic diseases.

Interest in this subject has recently been much aroused by the writings of Bossi of Genoa, who takes the ground that psychoneurotic manifestations even up to the point of suicidal mania are the direct necessary result of material changes in the genitals. Bossi regards the minor pelvic lesions as much more responsible for these neuroses than the more serious gross affections. For example, he states that the most important factor in the case is the forward or backward displacement of the uterus with the consequent "in-

fectious endometritis." The outbreak of psychoneuroses
up to the point of suicide at the time of the genital functions
he declares to be the result of increased "production and
absorption of toxic elements."

The absurdity of this doctrine needs little comment, the
wonder being that it has attracted so much attention. It
may only be remarked that infectious endometritis is a
rare disease outside of the septic puerperium and under no
conditions is it caused by simple malpositions of the uterus.
The doctrine is therefore founded on an entirely erroneous
pathological hypothesis. The writings of Bossi have been
valuable, however, in bringing out much excellent discus-
sion of this important subject more especially in the German
periodicals. The most illuminating of these papers have been
produced by Max Walthard who made his observations in
the clinic of the celebrated neurologist Dubois. (Prakt.
Ergebn. der. Geb. und Gyn. Jahrg. 2, p. 251 and Zentr. f.
Gyn. 1912, No. 16.) Walthard calls attention to the fact
that the old idea of a specific intimate nerve connection
between the organs of generation and the brain can no longer
be held and shows by a series of cases that the so-called gen-
ital psychoneuroses, (i.e., neuroses in which the mind is
fixed on sensations of the pelvic area) are found almost
equally in women with sound genital organs, in women with
diseased pelvic organs, and in women who have had them
entirely removed. Walthard after describing the manner
in which nervous symptoms may be produced by cortical
irritation of chemical poisons resulting from digestive dis-
turbances, bodily exhaustion, disorders of glands of internal
secretion, etc., advances the theory that a pathological
mental habit may in like manner produce an irritability of
the nervous system and cause symptoms similar to those
from functional bodily disturbances. The pathological
mental habit is according to Walthard primary. The patient
viewing every new sensation through her mental microscope

refers it to a floating kidney, a misplaced womb, an inflamed ovary or to some operation which has caused her the loss of her organs. The sensations are greatly exaggerated and in the words of Walthard an "overvaluation of their significance is placed upon them." These patients are, according to him, subjects only for psychotherapy.

Walthard's ideas are not of course in any sense new; but they deserve much credit for forcing the narrow-visioned gynecological specialist to realize that there is a vast new field of psychotherapy of which in the past he has taken little account. It is difficult for the average practical surgeon to appreciate fully the psychic element of his cases. Neurological parlance is ordinarily vague and uninteresting while the psychoneurotic manifestations of surgical patients are regarded as a necessary annoyance which must be avoided as much as possible.

No neurologist to my knowledge, has had greater success in mental therapy than has Dr. Austen Riggs of Stockbridge. In his admirable pamphlets entitled, "Talks to Patients," Dr. Riggs presents the problem of nervousness in an especially graphic form and as these pamphlets are not published I shall take the liberty with his permission to make some quotations from them.

Dr. Riggs pictures the field of consciousness as a great sea of immeasurable breadth and limitless depth. The surface of this sheet of water is covered with waves. Each impression made upon our consciousness from the time of birth to the present moment is represented by a wave, and the waves are arranged in groups and systems according to the laws of association.

"Now assume that the whole sheet is in total darkness, save that at or near the middle portion there is a light suspended from above, which illuminates a very small area. It is a mere pencil of light, capable of illuminating but one wave at a time, but it has the faculty of very

rapid motion, and is thus capable of illuminating a good
many waves in such quick succession that it produces
the effect of having illuminated them almost simulta-
neously. This light represents the attention. To carry
out the figure, we must imagine ourselves suspended
above it and as being able to control its direction by our
will. Just as the searchlight of a battleship has a definite
range beyond which the light does not reach, so the
light of our attention can be projected over only a lim-
ited area of the sea of consciousness. All that lies outside
this area, at any given moment, is, for that moment,
subconscious, — so that we speak of that portion of
consciousness outside the range of the attention as the
sub-consciousness and that portion which lies within
the illuminated area, as the *consciousness* or more ac-
curately, — the former is called the *unaware* conscious-
ness and the latter, the *aware* consciousness." ("Talks
to Patients," Elementary Mental Mechanics.)

. . . .

"Most of the time, the vast majority of these waves
stay quietly in the sub-conscious region, while only a
small minority pass in and out of the aware region; but
under certain circumstances a great many may obtrude
themselves into the illuminated area, and when this
happens, trouble promptly ensues.

Each family of waves may be said to be made up of
two sub-groups; one of which, comprising the waves
representing the sensations of position, of vibration,
and the deep muscle and tendon sensations, is a stable,
stay-at-home cluster which normally always remains
in the sub-consciousness. The other sub-group, which
includes the sensations of touch, pain, and temperature,
is more mobile, more loosely held together, and thus
any of its members are easily drawn from the family
circle into the aware region. Any of these mobile sen-
sations become very easily accentuated by the ordinary
physical stimuli of the environment and are thus con-
stantly flashing in and out of the attentive region. Even
without physical accentuation, one or more of them
may be drawn to the attention if one simply thinks of

this or that part of one's body, and consequently, at once becomes super-conscious of it.

Bearing this mechanism in mind, it is easy to see that sensations of this class, after being repeatedly picked out and dwelt upon by an otherwise idle attention, will form a most unwelcome habit of finding their way with greater and greater ease into the aware consciousness and that consequently they will become exaggerated through repetition and over-attention. This process, in fact plays an important part in the genesis of hypo-chondriasis, where the sufferer becomes abnormally aware of many, one might almost say of all of his sen-sations; and it also plays no small role in numerous other sorts of "nervousness."

There is another accident which may occur in the mental field which produces a similar result. Not only may the mobile sensations of the "touch" class, of which we normally may or may not be aware, become accentuated and exaggerated, but even those sensations of which we are normally never aware, namely those belonging to the stable, sub-conscious group, may under certain circumstances, reach the light of our attention. This they do by virtue of a process of disassociation, — that is by a breaking up of the normal arrangement of sensations in sub-groups and families. Thus when a family of sensory waves becomes accentuated, (although usually only the more mobile sub-group of the touch and pain class is affected), provided that the mental constitution be liable to disassociation, the lightly bal-anced associative values of a whole family may be upset. The result is that one or more sensations of the stay-at-home group, which should have remained quietly at home in the sub-consciousness, now disassociate themselves from this their normal cluster, and promptly join the other sub-group of the family. They then assume the habits of their new companions and wander with them into the illuminated area. Thus not only does the "touch" sensation become prominent, but it drags with it into the aware field one or more of its nor-mally sub-conscious brothers. Here of course the latter literally "make a sensation." They wear the uniform,

let us say, of the knee family and are therefore recognized as hailing from the knee country; but this is the only familiar characteristic they possess, and they are above everything fascinating to the attention because of the utter strangeness of all their other qualities. They are out of place, — as startingly out of place as fish out of water. The sensations are perfectly normal in themselves but they are distinctly and markedly abnormal in their relative position in consciousness. Like deep-sea creatures suddenly hauled gasping to the surface, they are out of their natural element, the quiet sub-conscious regions, and are showing themselves in the utterly strange environment of the intensely active and brightly illuminated aware region. Of course they seem unnatural, undesirable; and furthermore, we treat them with fearful attention and respect, because they seem to signify that there is something very strange going on in the bodily region from which they emanate. The sufferer little realizes that their abnormality consists chiefly in mal-position and not in intrinsic quality or significance.

Once having gained the *entré*, the dislocated sensations in question very soon acquire the habit of calling with always greater frequency and familiarity. Naturally the attention dwells with greater and greater intensity upon its strange guests, and the latter consequently swell to an enormous importance. Before long the secondary physical results make their appearance. The function over which the sensations in question formerly presided without let or hindrance, now suffers over-stimulation or over-inhibition as the case may be. The sensation, because of its abnormal activity and also because of its mal-position in consciousness, has attracted more than its share of the attention and the latter consequently interferes with the nervous control of the function." ("Talks to Patients" II, Nervousness.)

Let us now turn for a moment from this fascinating and poetic realm of the consciousness to the practical unimaginative gynecologist with an office full of nervous patients each with some real or supposed pelvic trouble. "What,"

he asks in confusion, "am I to do with these patients? Shall I send them all to the neurologist for mental treatment? I have tried that before and he does not seem to get any better results with them than I do."

Assume that we have a nervous patient before us who after seeing many consultants has been sent to the gynecologist as a last resort. We examine the abdomen and find say, a floating kidney or a retroverted uterus. Unless absolutely definite, painful or discomforting symptoms can be assigned to the condition found, gynecological treatment will do the nervous patient no good, but will actually do her harm by introducing to the searchlight of her mental attention new and strange sensations, thereby still more complicating her troubled and suffering consciousness. Such a patient therefore is not for the gynecologist even though she has a gynecological lesion, but is rather a typical case for psychotherapy, in the absence, of course, of other purely physical disabilities.

Assume now another patient who was a healthy, normal individual, say until the birth of her second child, which she describes as a difficult labor. This patient exhibits the same nervous symptoms that the first showed excepting that in the present case there are some symptoms very definitely localized in the pelvis, such as a sense of weight and pressure on standing, sacral backache, a leucorrheal discharge, etc. We examine the patient and find a uterus enlarged, retroverted and somewhat prolapsed. There is relaxation of the vaginal outlet, and an eroded lacerated cervix. Such a case is distinctly for operation. Every link of the broken chain of pelvic support is mended and the improvement in the entire nervous mechanism is astonishing. In this case the pain and discomfort of the pelvic family of sensations kept the searchlight of the attention continually flashing upon them and disarranged the entire central regulating system. The gynecological operation relieved the discomforting pain,

allowing the pelvic sensations to recede to the dark recesses of the unaware region where they belong, with a consequent automatic restoration of the central mechanism to its normal condition.

Assume now still a third patient similar in every respect to the one just cited excepting that there is a hereditary predisposition to neuroses, and that the duration of illness has been considerably longer. In other respects the symptoms are much the same. A gynecological operation is performed. The patient is relieved of her local pelvic symptoms, but continues to be as nervous as before, and now perhaps rivets her attention on some group of sensations which before the operation were of secondary importance, localized now for example, in the muscles of the neck. In this case the operation was justifiable and entirely indicated. The relief caused by the recession of the pelvic sensations is not sufficient to bring about an automatic self-regulation of the central mechanism. The hereditary predisposition and the long duration of the disease are factors which prevent the patient's regaining the proper control of the searchlight of attention. This case then illustrates what the neurologists call "habit neuroses." The patient is now a subject for the neurologist, and with proper discipline and suggestion may become entirely cured. Such a cure, however, is made possible, or at least far more likely by the surgical operation.

We have then three well defined types of nervous patients who consult the gynecologist. First, those in whom there exists a gynecological lesion which is not giving local symptoms and which probably has nothing to do with the nervous condition. Second, those in whom a gynecological lesion is the undoubted irritating cause of the nervous condition and, Third, those in whom a gynecological lesion is a contributory source of irritation to a generally abnormal nervous state.

There are of course, numerous complications and combinations of these three types. The most important of the

complications is the element of pathological mental suggestion. Thus a woman who has suffered long the constant nagging pain of pelvic inflammation is always nervous. If, however, she be told that the pelvic inflammation is the result of gonorrhea the nervous symptoms are many times increased. In the same way a patient who is suffering from long continued menorrhagia usually becomes very nervous; but she becomes much more so if there is added to the physical irritant the haunting apprehension of cancer. And so the instances might be multiplied.

We may summarize our conclusions of the relationship between minor gynecological lesions and functional neuroses by saying that: pelvic conditions which cause constant irritating, nagging pain or discomfort eventually produce neurotic symptoms, which are greatly increased if there be added the element of pathological mental habit with consequent overvaluation of the local sensations. There is, however, no mysterious or specific connection between the genital organs and the central nervous system. There is on the other hand between the two, exactly the same relationship that exists between the brain and every other area of the body, and the laws of pathological action and reaction are exactly the same. As proof of this a constantly irritating cholecystitis, or duodenal ulcer, or enteroptosis, or intestinal adhesion, or chronic appendicitis may produce a neurotic individual who does not in any way differ from the genital neurotic excepting that the searchlight of her mental attention is directed on a different group of sensations. Nor is this type of case confined entirely to those suffering from internal diseases. One of the worst male neurotics I ever saw is a man who was prevented from rowing on his college crew by a chronic synovitis of the knee. For many years his knee has occupied his chief attention. We are all of us only too familiar with the individual whose whole active consciousness is centered chiefly around an eczematous

umbilicus. In all there is the irritating discomfort, the pathological mental habit of the attention, and the overvaluation of sensations.

MENOPAUSE SYMPTOMS.

A consideration of the menopause symptoms is one of much importance in our present discussion for there exists on this subject a very wide divergence of opinion both among the laity and among the profession. We are concerned chiefly with the artificial menopause which results from hysterectomy and castration. I have treated this subject in a recent paper entitled, "Influence of the Ovary as an Organ of Internal Secretion." (Amer. Jour. Obstet., 1913.)

"There are those who regard the extirpation of the ovaries as provocative of the most serious postoperative psychoneuroses, while on the other hand there are many who believe that the removal of the ovarian secretion has an inappreciable influence on the physical welfare of a woman and that in certain neurotic conditions it is actually beneficial. In order to test this point I wrote a number of letters to my patients who had undergone supravaginal hysterectomy with removal of both adnexa. Each patient was asked the following questions:

1. Whether or not she had suffered from hot flushes?

2. Whether she had been more nervous or less nervous since the operation?

3. Whether there had been any change in her sexual feelings?

4. Whether or not she regarded herself improved in health by the operation, and to what extent?

To this set of questions 136 answers were received. The operations represented in this list were all supravaginal hysterectomies, with removal of the ovaries, although in a few of them there had been an implantation of ovarian tissue. The operations were mostly for fibroids, pelvic inflammation and double ovarian disease.

Of the 136 patients sixty-six had suffered from hot flushes for a few months, forty-two had had them

slightly, but were not seriously troubled by them, twenty-eight did not have them at all.

This question was put in order to determine the amount and duration of the symptoms of the artificial menopause on the theory that the presence of hot flushes is the most accurate index of this condition. The general impression gained from these figures was that the artificial menopause from hysterectomy and castration is shorter and less severe than is the natural menopause.

In answer to the question whether the patients were more nervous or less nervous after the operation, ninety-six reported that they were less nervous than before, while forty reported either that they were just the same as before, or that they were more nervous. If 70 per cent of castrated patients state that their operation has made them less nervous than they were when they had their ovaries, it does not seem as if the removal of the ovaries could have any great specific tendency to produce psychoneuroses. Of the forty patients who said they were more nervous than before the operation, or that their nerves were the same as before, thirty-three said that their general health had been improved, so that their nervous condition could not be said to be serious. Of the seven patients who said that their general health and nervous condition were both made worse, four were long-standing cases of pelvic inflammation who had had previous conservative operations, and who were markedly neurotic before the operation. The other three cases simply stated that they were more nervous, and that their general health was worse than before operation. In one of them the cause was found to be due to rheumatism, and in another it was due to a postoperative hernia of the wound. These figures would compare favorably with those of any other serious surgical operation, in which unquestionably nearly an equal percentage would report an increased nervousness after the operation. Definite severe psychoneuroses traceable directly to the loss of ovarian secretions have not come under my notice. The real causes for the serious postoperative nervous complications can usually be found in such lesions as postopera-

tive pelvic adhesions, postoperative hernia, incomplete support of the pelvic floor, wound infections and other results of unsuccessful surgical technic, which leave the patient in an uncomfortable or painful state."

In analyzing the artificial menopause symptoms it is necessary to divide them into two very distinct groups. Namely, the vasomotor and the psychoneurotic.

The vasomotor symptoms are represented in general by the so-called hot flushes. These appear in at least 80 per cent of castration cases.*

The vasomotor disturbances do not usually produce nervous symptoms unless they are very severe or frequent, in which case they sometimes react seriously on the nervous system in the same way as any other physical irritant.

Psychoneuroses as distinguished from vasomotor disturbances are by no means definitely consequent on the loss of the ovaries. On the contrary psychoneurotic conditions are again and again relieved or completely cured by a hysterectomy operation which has relieved the patient of some painful irritant like that for example of a pelvic inflammation.

Severe psychoneuroses may follow hysterectomy; but they are brought about in the following ways. The operation may have been misdirected and not indicated in the first place, or it may have been improperly performed or surgical complications may have ensued which have left the patient in a painful, uncomfortable state. As proof of this is the fact that postoperative neuroses following hysterectomy were formerly far more common not many years ago than they are now. This can only be explained on the ground that the technique of the operation has in the last few years

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* The cause of hot flushes is not known, though recent investigators such as Schickele and others ascribe them to a heightened blood pressure due to the removal of the vasodepressor influence of the ovarian internal secretion. Observations made at the Free Hospital for Women by Miss H. J. Ewin and myself in a series of about 50 cases have failed to reveal a single instance of increased blood pressure.

been very greatly improved so that now if it is properly done
there is no shock, no bleeding, no postoperative prolapse of
the vagina, no pelvic adhesions, and other unfortunate com-
plications, which if present, cause nagging discomforts that
are sure to disarrange the nervous mechanism.

Another important cause of the psychoneuroses of the
artificial menopause is that resulting from mental suggestion.
Under normal conditions a woman does not instinctively
suffer a sense of physical degradation from the loss of her
pelvic organs especially if such a loss is attended with a
relief of pain. This sense of degradation may, however, be
very powerfully induced by the criticisms of an unfeeling
husband or the suggestions of unwise friends by which the
patient is led to contemplate her inability to bear children
or to fear the loss of youth and the premature onset of old
age. Under such conditions the mental distress may result
in severe psychoneuroses. Such a state, however, must be
regarded as due to psychical irritation and not in any sense
as a specific consequence of the loss of ovarian secretion.

What has been said concerning the nervous disturbances
of the artificial menopause is also true of the physiological
menopause in which vasomotor and psychoneurotic symp-
toms may appear. Dubois after studying many cases for
a period of more than thirty years has come to the conclusion
(Monatschr. f. Geb. u. Gyn. Feb. 1913) that the neurotic
manifestations are largely due to mental suggestion, as a
result of the cares and worries and apprehensions that are
usually incident at the period of the climacteric.

GYNECOLOGICAL DISEASE AND THE PSYCHOSES.

On the subject of the true psychoses in their relationship
to gynecological disease I cannot claim to speak with great
authority on account of a limited experience with cases of
this kind and on account of lack of familiarity with mental

disease. Nevertheless I have had a number of instructive cases from which conclusions of some value may be drawn. The series which I have chosen to illustrate this subject consists of fifteen psychosis cases in which the operation of hysterectomy with castration was performed. All of these patients were suffering from some gynecological disease such as pelvic inflammation, fibroids, or severe dysmenorrhea. In all there were serious exacerbations of symptoms during the menstrual period, and in some the symptoms appeared only at that time.

The mental conditions represented were as follows: Hysteria, five cases; epilepsy, four cases; insanity of the melancholic or depressive type with suicidal tendency, five cases; dementia precox, one case.

Of the five hysteria cases three were much improved and two may be regarded as perfectly well. One of the cases which is entirely cured suffered from incessant epileptiform seizures which could with difficulty be distinguished from true epilepsy. The operation was for extensive pelvic inflammatory disease.

Of the four cases of epilepsy there have been no cures; but all have been improved, two of them markedly so and the other two moderately.

Of the five melancholic or manic-depressive cases, all have been very distinctly improved, while one is completely well though her mental condition before operation was the least promising, suicide having been twice attempted.

The dementia precox case was improved temporarily; but has since lapsed to her former condition.

It is sufficiently evident from this small series of cases that the performance of gynecological operations cannot be expected to cure true psychoses, but they may greatly improve the mental condition by removing the pelvic irritation of pain and discomfort, while in certain cases, which from the

standpoint of the psychiatrist are essentially curable, operations may greatly facilitate or hasten a complete cure.

I wish to say in conclusion that the remarks made in this paper touch only in a most superficial way a subject of the widest importance and one capable of very great development. It has been my desire chiefly to emphasize the point that there exists no mysterious or peculiar nerve connection between the female genital organs and the central nervous system, and that disturbances in the former cause manifestations in the latter by the irritation of pain and discomfort. It seems to me that if this simple theory be borne constantly in mind in our practical treatment of patients there will be fewer mistakes on the part both of the gynecologist and the neurologist.

DISCUSSION OF ARTICLE XVI.

DR. W. L. BURRAGE, Boston: I feel in the same position as Dr. Hubbard. I prepared a discussion and in many ways I suppose I should not read it after hearing Dr. Graves's very interesting paper which covers the ground so well.

However, my opinion is rather different from his in some respects, and my experience dates back a little further, so I am going to read it.

Soon after the birth of gynecology as a specialty, in the year 1880, B. S. Schultze, of Jena, in discussing the effect of displacements of the uterus on the nervous system* made this statement:

"Nervous affections caused by reflex action from the uterus through the nervous centers, reveal their connection with the displacement by their disappearance coinciding with its removal. I have often observed a nervous headache depart immediately and forever, on the reposition of a retroflexed uterus, and I do not mean headaches only called nervous because their cause was not known, or in the sense that every pain is nervous, but properly diagnosed trifacial vaso-motor neuralgia,

* *Displacements of the Uterus*, English Edition, p. 249.

cases of hemicrania which had existed for years, had exhibited paroxysms regularly several times a week, and which had been most vigorously treated in the orthodox manner without any benefit whatever."

Thomas Addis Emmet, pioneer gynecologist in America and originator of the operation of trachelorrhaphy, said in 1883* with reference to the effect of scar tissue situated between the lips of a lacerated cervix:

"I do not assert that the general health of every woman who has a scar in the cervix will suffer, or that she will always have neuralgia in consequence. But it has been demonstrated to my mind as clearly as anything we accept as truth in medicine, that there exists a relation of cause and effect under the following circumstances. If a woman receives an injury in labor, as a laceration of the cervix, and is in such perfect health as to be able to withstand the irritation, she may go for an indefinite time without suffering any evil consequences. But if she should ever become anemic, with this condition of the cervix, she will either be a victim of neuralgia, or will not recover her health until the source of the irritation has been removed by the surgeon, or by nature after she has gone through the change of life."

He refers to the greater prevalence of "neuralgia" among women who, in the previous years, had had their torn crevices treated by the application of nitrate of silver.

The intimate relationship between disease of the genital organs in women and nervous and mental disease became more apparent from year to year. In 1889, W. P. Manton of Detroit was appointed gynecologist to the Eastern and Northern Michigan Asylums for the Insane. As far as known this was the first appointment of a trained specialist in gynecology to care for the local troubles of the women inmates of an insane asylum. At the present time, it is the general custom to give uterine disease proper diagnosis and treatment in asylums for the insane as well as in general hospitals. After twelve years' experience in the treatment of the insane, Manton wrote: †

* *Principles and Practice of Gynecology*, p. 636.

† *Transactions, American Gynecological Society*, 1901, pp. 383–391.

"Lesions of the pelvic organs are important factors in the production of insanity in those of unstable mental organization, *in the presence of co-existing conditions which themselves tend to impair the mental integrity;*" also: "In not a single asylum case could insanity be traced solely to abdomino-pelvic disease. Nor have I witnessed a single recovery from mental disease following surgical operation in which the cure could be attributed to the operation alone."

This experience contrasts with the findings of A. T. Hobbs* in the London (Ontario) Asylum for the Insane during the five years ending in 1902. Among 1000 cases, he found 253 with gynecological lesions. All of these were operated upon; five died, 100 were cured, and 59 improved as regards their psychoses.

During the years that the gynecologists were solving the problems of the repair of vesico-vaginal fistula, lacerated cervix, and ruptured pelvic floor, while at the same time giving to the profession aseptic abdominal surgery, the neurologists were studying and classifying functional nervous diseases. In the eighties, the term "hysteria" comprised a very large proportion of all the functional nervous disorders. At the present time, hysteria is regarded as relatively uncommon in America. At first, a certain number of the functional neuroses formerly classed as hysteria were grouped under the new disease, neurasthenia; and today, many which formerly were classed as neurasthenia come under the title, "psychasthenia."

Following the classification and definition of such well-known neurologists as Charles L. Dana and Lewellys F. Barker, hysteria may be defined as increased susceptibility to suggestion. It is a transmissible neurosis affecting adult women more often than men in the proportion of four to one. Its stigmata are: anesthesias, anamnesias, abulias, and alterations of character; its accidents are: crises, paralyses, contractures, and delirias.

Neurasthenia is "irritable weakness." This also has heredity as a predisposing cause, and is found most often among the highly cultured, and is slightly more frequent

* *Buffalo Medical Journal*, 1902.

in men than in women. Exciting causes are: mental strain, shock, sexual abuse, infectious fevers, alcohol, syphilis, and autotoxemia. Its chief symptoms are: headache or sense of pressure in the head, backache, sleeplessness, depression of spirits, disturbances of digestion, of circulation, and of the genito-urinary organs, such as anomalies of menstruation, frequent and painful micturition, and abnormalities of sexual desire or sensation.

Psychasthenia, a term suggested by Janet, is an obsession or fixed idea that consciously affects the mind. The most frequent etiological factor is heredity, just as in hysteria and neurasthenia. It occurs equally in males and females. The exciting causes are: shock, accident, alcohol, infectious fevers and uterine disorders. The symptoms are: a sense of incompleteness or feelings of unreality which dominate the patient. From these develop obsessions, impulses, fears, or dissociated personalities. The impulses often have to do with some criminal act, but the patient seldom yields to them. Other common symptoms are: a persistent sense of boredom, a tendency to over-exert in order to distract the mind, indifference to things in which the patient was formerly interested, premonitions of impending disaster or of going insane, or of having a dreadful disease.

Of these three common psychoneuroses, as they are called, it is plain that hysteria alone occurs more frequently in women than in men; and because in this disease, some neurosis or psychosis can be discovered in the parents of 75% of the cases, it is probable that the contention of the neurologists that the condition of the uterine organs has no etiological significance is well maintained.

Leaving out of consideration epilepsy, hypochondrias, the relatively rare traumatic neuroses, and the organic nervous diseases which have some association with, or are mistaken for, gynecological disorders, such as beginning tabes, Graves's disease, and multiple sclerosis, we come to a discussion of the modifying influence of uterine disease on hysteria, neurasthenia, and psychasthenia.

In Supplement VII to Nothnagel's *Special Pathology and Therapeutics*, published this spring, there are 162 references to the literature on the relation between pelvic disease and hysteria and neurasthenia, so that the claim cannot justly be made that the subject has been slighted.

Maria Tobler of Florence published an important article in the *Monatschrift für Geburtshilfe und Gynäkologie* in 1905, in which she reported conclusions gained by a study of 1020 women in her clinics during a period of two years. She found 137 of this number, or 13%, had psychic disturbances accompanying menstruation. Of these, 80, or 7.8%, had menstruation without any discomfort whatever; and 44 of the 80, or 59%, when examined, proved to have a normal uterine condition, while the rest showed a variety of gynecological affections. Fifty-seven women, or 5.6%, had painful menstruation accompanied by such symptoms as headache and nausea. These experienced only depression of spirits or excitability during menstruation. Among these 57, the uterine state was reported as normal in 23, or 40%.

Altogether, among 1020 women investigated, 137, or 13%, had psychic disturbances with menstruation; and in 49.5% of these, the uterine condition was recorded as being normal. In other words, half of all the women having mental symptoms at their catamenia had normal pelvic organs. This means a good deal, for we have no reliable statistics of the incidence of normal uterine organs among healthy and sick women in general, and it is supposable that a considerable number of all women would be found to present some sort of uterine anomaly if subjected to examination at the hands of trained gynecologists.

Tobler concluded that the menstrual period in our women of today means, in a majority of cases, a time of diminished sense of wellbeing and a reduced functional capacity; a condition which must be considered neither as fundamental nor necessary. It is the result of a degeneration of an impaired constitution and of a wrong manner of living, so that the increased products of metabolism, which are formed during the periodic stimulation of the genital system, instead of being used for the benefit of the body, become toxic. For many women suffer no pain with their catamenia; and in a not negligeable number, the menstruation time is subjectively a period of increased vital energy, when the organism is, theoretically, in condition to form and develop a new being.

To the unravelling of some of the twisted skeins of the interrelation of gynecological and nervous diseases, Max Walthard, of Frankfort, contributed a thoughtful paper in

the *Praktische Ergebnisse der Geburtshilfe und Gynäkologie*
in 1910, and followed it by an article in No. 16 of the *Zentral-
blatt für Gynäkologie* for 1912. He thinks that only when a
patient's attention is called to the fact that she has gyneco-
logical disease, — some symptom, such as pain or leucorrhea,
having made her conscious of local trouble, — and she over-
values this fact of uterine impairment, does pelvic disease
cause psychoneurotic conditions and manifestations.

In Walthard's clinic, he found that 400 women out of 3000
who had consulted him, had sound pelvic organs and func-
tional complaints only. In 5% of these, the functional
disturbances were considered as psychoneurotic genital
symptoms.

We must agree with him in the statement that only the
etiological treatment of psychoneurosis, — that is, a com-
plete change of the pathological mode of thought; a more
judicious and reasonable valuation of the gravity of the
disease, — can bring about a final relief of psychoneurotic
symptoms.

Bossi, of Genoa, startled the medical fraternity by de-
claring in the *Zentralblatt für Gynäkologie* in 1911, No. 36,
that in his opinion not less than half the suicides among
women are of gynecological causation. He found a tendency
to suicide more frequently in cases with relatively slight
uterine disorders than in those having severe lesions; and
he observed it mostly in cases of chronic metritis associated
with displacements. Therefore, he concluded that any intox-
ication or poisoning of the system causing nervous or psychic
phenomena, has a gynecological origin and that curing pelvic
disease is a sure prophylaxis against suicide. Beyond the
report of seven illustrative cases, no further proof of his con-
clusions was given. In a second paper* he reported four more
cases.

E. Siemerling's† comment, namely: that some of Bossi's
instances of cure were due to suggestion, and that suicidal
mania is only a symptom of a severe neurosis or psychosis,
and not a disease in itself, strikes one as being sane and to
the point.

I should subscribe to Walthard's statement that "it

* *Zentralblatt für Gynäkologie*, 1912, No. 9.
† *Zentralblatt für Gynäkologie*, 1912, No. 13.

behooves us gynecologists to treat healthy genital organs less
often in the presence of psychoneurotic manifestations; and,
moreover, we should recognize these manifestations as
functional symptoms and refrain from any form of local
treatment." Also: "It is worth while for the gynecologist
to become acquainted with psychotherapy, for in this way
the number of gynecological operations and local treatments
will diminish, and the number of successful results in gyne-
cology increase."

DR. S. RUSHMORE, Boston: I feel after this paper and the
discussion that there is really very little for me to say on the
subject.

The importance and significance of the subject which Dr.
Graves has presented is suggested by the fact that it is a
topic which persistently recurs for discussion; that while
there are times when very little attention is given to the
subject, there are other times when it arouses a good deal
of interest. That indicates two things: — first, that an
important relationship exists between these two systems,
the genital and the nervous; and second, that up to the
present time at least, there has not been a satisfactory ex-
planation of the correlation of the two systems. We have
two important elements, the nervous system and the genital
system, and several questions arise.

In the first place, if the genital system is diseased, what
effect does that have on the normal nervous system; if the
nervous system is diseased, what effect does that have on a
normal genital system; and if both are diseased, what are
their mutual and reciprocal relations?

The impulses which arise in the pelvis from the genital
organs, pass to the spinal cord; thence, by the spinal nerves
and sympathetic nervous system, to pelvic and abdominal
organs. By this route we have a subcortical reflex. In ad-
dition to this we have impulses which travel to the brain,
and through that we have what we may call a cortical reflex.
Now the importance of the subcortical reflexes we do not at
present understand. Most of us think that practically they
are of very little importance in giving rise to symptoms.
From time to time they have received a great deal of atten-
tion, but so far as the evidence goes they constitute a very

unimportant part in the symptoms which arise from gyne-
cological disease. More and more attention is being given
to those reflexes which have added to them the psychic factor,
and we have the numerous psychoneuroses which are asso-
ciated with gynecological disease. Of course the important
question is, what is the causal relation between the gyne-
cological disease and the disturbed mental state.

To understand that properly we have to go into the cause
of these nervous states in general, and we actually find that
while a certain proportion of them are apparently caused by
gynecological disease, they may arise from other conditions
also. Some mental disturbances are due to intoxications;
and, by the way, Professor Bossi's view is that many dis-
turbed mental states are due to non-septic intoxications
arising in the genitalia. Some of them are due to congenital
or developmental conditions. The interrelations of the glands
of internal secretion are coming to play a more important
part in our explanations of disease of both nervous and genital
systems.

Now there is one point which I particularly wanted to
emphasize in regard to their relations, and that is: — suppose
we find a case in which quite clearly these symptoms are due
to gynecological disease, and I am inclined to think that more
of these cases of psychasthenia and neurasthenia should re-
ceive operative treatment than has been suggested by Dr.
Graves, if we find such a case, the first treatment is operation,
but by the operation we do not cure the patient, though we
may relieve the anatomical condition. The patient is still
neurasthenic and must undergo the appropriate treatment,
which we should in no case forget or neglect.

ARTICLE XVII.

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OBSERVATIONS ON A SERIES OF NINETY-EIGHT CONSECUTIVE OPERATIONS FOR CHRONIC APPENDICITIS.

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By E. A. Codman, M.D.,
of Boston.

OBSERVATIONS ON A SERIES OF NINETY-EIGHT CONSECUTIVE OPERATIONS FOR CHRONIC APPENDICITIS.

What is a chronic appendix?

Pathologists deny the existence of chronic appendicitis. They say there is no evidence of any real condition of chronic inflammation and explain our surgical chronic appendices as healed or healing appendices.   The effects of previous inflammation are shown by:

1. Peritoneal adhesions (not congenital).

2. Obliteration of the whole or portions of the lumen.

3. Stricture of the lumen with more or less dilatation distal to it.

4. The presence of a hard concretion or foreign body. Such bodies are either retained by strictures or mechanically produce the same effects as strictures.

Every surgeon should read Aschoff's recent monograph on the Pathology of Appendicitis.   In brief he holds that the demonstration of obliteration proves a previous inflammation and that over 50 per cent of humanity have during their lives attacks of appendicitis.   He gives definite statistics on this point.   His book is thorough, logical and painstaking and leads to the inevitable conclusion that the appendix is always a menace and should be removed as a routine.

I believe that any surgeon who is willing to follow the facts to their logical conclusion will say, if he is not too much afraid of ridicule, that routine appendectomy is logical and reasonable for every child.   I can show you that it is far more logical and reasonable than our foolish attempts to

diagnose chronic appendicitis and on the ground of our
diagnosis to advise operation.   In addition to Aschoff's
statement just consider that out of one hundred abdominal
sections taken in a consecutive series at random from the
Massachusetts General Hospital records, 71 showed definite
lesions of the appendix, although no such preoperative diag-
nosis was made from the history.   And yet on the other hand
in my 98 cases diagnosed definitely as chronic appendicitis
only 61 showed pathologic evidence.   You may be able to
diagnose these cases better than we can, but I would like to
see you prove it.

I tell you that when you advise routine appendectomy
you are talking reasonably and when you attempt to advise
appendectomy on cases which have never had a definite
acute attack, because you have made a diagnosis of chronic
appendicitis, you are talking foolishly.

Your advice for appendectomy is more defensible on the
general ground that it is "six to one, half a dozen of t'other"
that your patient has or will have appendicitis, than it is on
the ground that you have made a diagnosis of chronic appen-
dicitis.   If you have seen your patient in an acute or sub-
acute attack, that is another matter but even then you must
expect to find at operation evidence of a healed or healing
appendicitis not of a chronic one.   You may shut the barn
door after the horse has been stolen.   For instance, if the
attack which you saw affected only the tip, that portion
would be found as a harmless obliteration, but if it was more
proximal and caused stricture then it would be a healing
appendix or practically a chronic appendix since inflamma-
tion tends to recur behind a stricture.   Personally, I believe
it may persist behind a stricture so that for all intents and
purposes a strictured appendix is a chronic appendix, and
is the form really most vicious.

Aschoff shows that bends and kinks in the appendix are
potentially the same as strictures.   It is an unusual appendix

that the surgeon cannot show to have at least a bend or a kink!

However, in this study I have not included bends, kinks, injected appearances, catarrhal appendices, or any doubtful irregularity or thickening as a "chronic appendix" but have held up definite peritoneal adhesions, strictures and obliterations as the standards of pathologic demonstration. Even adhesions and obliterations cannot strictly be called "chronic appendicitis" but for the sake of argument I have included them, although they are probably safer than the so-called normal appendices. Concretions, if hard, I have regarded as pathologic, but not so, soft, fecal masses.

In nearly every case I have myself cut the specimen in the laboratory and examined it with care. Dr. W. F. Whitney has made sections for me of over one-half the specimens. Together we have reached the conclusion that the microscope alone cannot make the diagnosis of a previous inflammation as well as the gross observation of the appendix in situ and on section. The presence of a stricture with more or less dilatation distal to it seems to me the one dangerous form of chronic appendicitis.

I have made several observations at the operating table which interested me a good deal but which I had never noticed before in the ordinary course of operating. One is that when the abdomen is first opened an appendix may appear long, large, flaccid and whitish like a dead fish worm, and yet when it is handled it contracts and shortens. Immediately tortuous injected blood vessels stand out on its surface. I have seen such appendices removed and claimed as pathologic.

Appendices after removal shrink one-quarter to one-third in length. This destroys histologic opinion founded on the thickness of the muscular coat. By tickling an appendix in situ at one spot, a local stricture can be produced which could easily deceive an audience.

This report differs from the usual surgical paper in that
the cases were studied with certain definite objects in view
and was not a compilation of statistics from purely fortuitous
observations.*

More than this, it inaugurates what I hope will prove
an important method of really scientific clinical observation
at the Massachusetts General Hospital, for poor as it is,
it forms a definite basis for comparison, so that future sur-
geons at the hospital who undertake succeeding series of
cases will have some standard to surpass.

The ideal chronic appendix operation should remove a
clearly pathologic appendix, which has been without doubt
the cause of the patient's symptoms. The operation should
be done without mortality, pain, vomiting, the faintest sepsis,
hernia, ugly or sensitive scar or other complication.

If a surgeon could do one hundred cases and fulfill these
conditions he could certainly qualify as an expert abdominal
surgeon. If at the same time he could contribute any im-
portant original observations on the subject he might add
himself to the list of great surgeons.

To show how far I fell short and to offer a record for some
junior surgeon to excel, I present the following remarks.

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* All the cases in this series were either sent into the hospital under the
diagnosis of chronic appendicitis or were so diagnosed in the hospital by
some other surgeon and then transferred to me.

After carefully taking the history and examining each case, if I considered
the symptoms as more probably due to some other organ than the appendix
I transferred the patient to the general service. Thus the fact that I ac-
cepted the cases in the series was an acknowledgement of agreement in the
diagnosis that the appendix was the most probable cause of the patient's
symptoms. Only about six cases were thus transferred and I regret to say
that three of these showed a chronic appendix at operation.

In a number of cases there was grave doubt in my mind as to whether
the patient really had chronic appendicitis and as my experience grew I
began to recognize the cases which were positive and those which were doubt-
ful, but even if not positive, I operated just as we all do when we consider
that the symptoms justify appendectomy.

I do not believe that I operated any oftener in doubtful cases than does
the average surgeon in private practice. In a few instances the patients
after hearing that a positive diagnosis could not be made, refused operation.
These cases were operated on between Dec. 1st., 1911 and June 1st., 1913.

All cases operated upon were diagnosed as chronic appendicitis but only sixty-one appendices had demonstrable evidences of having been inflamed.

In seventeen cases the real causes of the symptoms as determined after operation were probably as follows:

Chronic salpingitis.....................	2 cases.
Tuberculous mesenteric glands..........	3 cases.
Painful right inguinal hernia............	1 case.
Gallstones............................	2 cases.
Small ovarian cyst....................	1 case.
Tuberculous peritonitis................	1 case.
Congenital pelvic kidney...............	1 case.
Tape worm...........................	1 case.
Cardio-spasm.........................	1 case.
Megasigmoid..........................	1 case.
Ptosis and megaduodenum.............	1 case.
Appendix abscess.....................	1 case.
General syphilis......................	1 case.

But six of these seventeen cases also happened to have a chronic appendix.

In twenty-six cases the appendix appeared normal and may or may not have caused the symptoms. Even if an appendix shows no gross or microscopic evidence of an inflammation it by no means follows that it has not been the cause of symptoms. The mucous membrane of the nose, pharynx and tonsils may be severely inflamed, swollen and infected and yet return to a perfectly normal condition. Why should not an appendix which is abundantly supplied with active mucosa and lymphoid tissue likewise suffer acute inflammation with a purulent discharge and yet shortly return to a normal condition? Is it not reasonable to assume that most acute inflammations of the appendix discharge naturally into the lumen of the bowel? It is only when some

pronounced bend or kink retains the secretion that trouble comes. This is another argument for routine appendectomy, for it might save many ordinary belly-aches.

There was no mortality in any of the cases although besides appendectomy the following operations were also done.

1 Oophorectomy.	2 Herniotomies.
1 Nephrectomy.	1 Trachelorraphy.
1 Cholecystostomy.	2 Ventral suspensions.
1 Fibroidectomy.	7 Operations for Lane's
1 Pyloroplasty.	kink.

Only eight patients (and these were done under anoci association) had practically no pain. Only eleven cases were recorded as having no vomiting although in twenty-eight cases no vomiting was recorded.

There was no serious sepsis but in eighteen cases first intention was not absolutely perfect, varying from a slight ooze of serum to a slight purulent discharge (only four cases). Such sepsis is not individually serious but shows an imperfect technique, which might be serious in more grave cases.

Therefore, the next student of chronic appendix cases still has problems of diagnosis and technique to meet. I should have felt badly about my diagnostic skill had not my colleagues removed an equal number of chronic appendices during the same period from cases which they had diagnosed as gallstones, gastric and duodenal ulcers, retroversion, acute appendicitis, etc. We have now adopted a habit of writing down preoperative diagnoses so as to make these mistakes a little more personal.

Before starting this series I wrote down ten distinct objects of the investigation, the most important of which were as follows:

No. 1. To find a set of symptoms constant enough to justify diagnosis.

No. 2. To find the relative frequency of

(a) Constipation.

(b) Intermittent diarrhea.

(c) Hyperacidity symptoms.

(d) Dyspepsia in general.

(e) The kind of pain.

(f) The hyperesthetic zone.

(g) Dilatation test.

No. 3. To make observations on prolapsed and redundant ceci with long mesenteries. (Jackson's veil, etc.)

No. 4. To make observations on Lane's kink.

No. 5. To try Crile's anoci association with novocain and quinine urea for post operative pain.

No. 6. To find means to make the convalescence more comfortable.

No. 7. To improve the operative technique in

(a) Avoiding adhesions.

(b) Speed of operation.

No. 8. To teach the operation to house officers.

No. 9. To obtain statistics of absolute asepsis.

No. 10. To obtain X-ray data on Bismuth meals.

I will take up the answers in order.

No. 1. As to diagnosis:

There were two fairly distinct symptom complexes.

(a) The true appendix sequence. Cases which have had a number of previous attacks lasting a few days — not hours. These attacks are characterized by epigastric or general abdominal onset and right iliac localization of pain followed by gradually subsiding tenderness after the pain has gone. In the interval between the attacks tenderness at McBurney's point may be absent. These cases seldom have habitual constipation.

They show definite appendix strictures, obliteration, or adhesions.

(b) The pseudoappendix sequence.   These cases have right sided pain in the appendix region which is frequent, usually daily, though intermittent.   There is general right-sided tenderness, especially at and about McBurney's point. They have no long interval of freedom.   The attacks are mild and not often feverish.   They are constipated and usually have the other stigmata of visceral ptosis.

At operation large, long, free, flaccid appendices usually containing soft fecal material are found.   In addition various local anomalies such as *cæcum mobile*, Jackson's veil and Lane's kink are usually evident.   These cases are not often permanently relieved by removal of their appendices although at first they enjoy the experience of recovery from the operation.

Next year I hope to present accurate reports of the end results of these two groups, for by classifying these cases now and following them up later, I can compare the results.

No. 2. As to individual symptoms:

In the sixty-one definite appendix cases constipation, usually not habitual, was present in only 21 cases and in eight of these mobile ceci were also present.   But in four cases no note was made.

In the thirty-seven cases with normal appendices sixteen were habitually constipated.   In asking the questions about constipation I was particularly careful as I was myself astonished at finding how seldom it was a symptom of chronic appendicitis.   It almost seems as if the presence of a strictured appendix irritated the bowel enough to prevent constipation, while on the other hand in the cases with large flaccid appendices the stimulus was absent.   This point may be proved or disproved by the next investigator.

Diarrhea, persistent or intermittent, occurred in only nine cases out of eighty-seven recorded and can no longer be quoted as a symptom of chronic appendicitis, but when present in a doubtful case is in favor of a diseased appendix,

because eight of the nine were among the sixty-one true chronic appendices.

One of the things that interested me most, was that dyspeptic symptoms especially the hyperacidity form which we now consider the cardinal symptom of duodenal ulcer, were found at all severe in only twelve cases and were vaguely present in only twenty-five more.

Of these thirty-seven, *cæcum mobile* was also found in twenty-two. This suggests that the para-appendiceal conditions may be the cause rather than the appendix itself.

The hyperesthetic zone test was most disappointing as a rule, although in a few instances it was very positive. It was negative where it should have been positive thirty-seven times and *vice versa* ten times, in seventy-one observations.

The dilatation test which consists in inflating the colon with air and thus exaggerating local pain and tenderness was occasionally of value especially where there was a condition of subacute inflammation. It was positive twelve times when it should have been negative and *vice versa* fourteen times, in sixty-one observations.

No. 3. I have not yet convinced myself that the various operations recommended for *cæcum mobile*, pericolic membranes, Jackson's veil, etc., are worth doing. Therefore, in this series I determined to wait until a year had passed after appendectomy before recommending any surgical treatment for these conditions. Next year these results will be reported. Suffice it now to say that in sixty-seven cases where the mobility of the cecum was noted it was found long enough to pull out of the wound easily in forty-two cases. In twenty of these the appendix was normal. Jackson's veil was found in thirty-seven out of seventy-one cases.

At the end of the series I came to the conclusion that he who operates on Jackson's veil or *cæcum mobile* is likely to find many cases.

Lane's kink was present twelve times and in seven cases I did the usual plastic operation without much faith, but believing it might do good and was not likely to do harm. The results will be reported next year. I am inclined to think that they will not be favorable.

No. 5. As to the comfort of the patient:

It took two trips to Cleveland to convince me that Crile's anoci association technique was worth while. Twenty-five cases were done more or less perfectly by this technique and the more perfect the technique, the better the result. A few cases really had no pain at the time of the operation or after it. Though not directly connected with this subject, I may state that I have done with this technique without shock, other difficult operations which I feel would have been fatal without it. In the hurry of hospital practice it is not used; but I believe that its general principles have come to stay in operations for chronic appendicitis and most others.

There is no question but that it renders the convalescence far easier. If it fails it means lack of care on the part of the surgeon.

No. 10. As to the value of the X-ray:

In fifty cases I have carefully studied the X-ray plates which Dr. Dodd was kind enough to take of these patients with Bismuth meals. Careful study of the plates justifies the conclusion that the X-ray is of considerable help in the diagnosis of chronic appendicitis, especially in differentiating the condition which I have called pseudoappendicitis or ileocecal anomalies. The lumen of the appendix distended with Bismuth was frequently seen.

Although this paper is brief and perhaps offers no new points of interest to you, I hope you will agree that the method which it illustrates is an important one. Great hospitals like the Massachusetts General Hospital have a duty to perform to medical and surgical science. Their

clinical material should not be used haphazard to perfect the skill of a few favored operators without scientific study of the cases. By grouping cases into series large enough to favor comparative study and by observing definite previously-determined points a rational clinical science can be established. By putting the results on record the patient will not only be protected, but each operator will have the strongest incentive to excel in all the details of diagnosis and technique which count toward a successful result. This method will put an end to the old experimental surgery where each operator took a try at each new operation and reported only the good results.

It will also discourage hasty diagnoses and thoughtless operating by busy men with great reputations. By making the opportunity to operate the reward of study of the cases, it will give the young surgeon a chance to educate himself as well as to advance the science of surgery.

For instance, when a technique is evolved so sure that no deaths, no pain, no vomiting, no hernia, no complications of any kind occur — then we can offer the best of arguments for routine appendectomy.

The Surgical Executive Committee at the Massachusetts General Hospital have it in their hands to answer this question by continuing to assign blocks of 100 cases of chronic appendicitis to individual surgeons until their statistics show that the ideal harmless, painless operation has been reached. Then routine appendectomy can begin, and the price will be cut to somewhere near its proper relation to the skill required.

POSTSCRIPT.

Suppose chronic appendicitis had not yet been described and some one offered the following arguments that it existed and he could diagnose it.

Ninety-eight cases were diagnosed as chronic appendicitis and at operation only 61 appendices showed evidence of ever

having been inflamed — and 50 of these should really not be included because they had definite histories of classical acute attacks.

Meanwhile (1½ yrs.) his colleagues and he himself operated on an equal number of abdominal cases under other diagnoses than chronic appendicitis and yet a "chronic appendix" was the only abdominal lesion they could find!

Another consecutive series of 100 laparotomies was taken, which were done for other lesions (chronic appendicitis not even being mentioned) such as retroversion, fibroids, gallstones or ulcer, and in which the condition of the appendix was recorded. This showed 71 "chronic appendices." A greater proportion than in the diagnosed cases!

Would these arguments be listened to if the disease were new? Would they be tolerated in any other branch of science?

And then the paradox that the pathologists say there is no such thing as chronic appendicitis!

Obviously this subject of "chronic appendicitis" needs revision and a new nomenclature. The writer suggests the following :

1. Terminal obliteration — The scar of previous inflammation is distal — i. e. begins at the tip and obliterates the lumen to a greater or less degree towards the base and therefore causes no obstruction. (Fig. 3.)

2. Strictured — The scar does not involve the tip and therefore has active secreting mucus membrane distal to it and hence presents delay to discharge of the contents. (Fig. 2.)

3. Kinked appendix — Cases in which the walls of the appendix are normal but in which the discharge from the lumen may be hindered by anatomical conditions outside of the appendix such as a contracted mesentery, congenital misplacement or post inflammatory adhesions. (Fig. 1.)

4. Chronic appendices — The so-called normal appendices in which the lumen is patent and neither hindered by stricture in the walls nor obvious kinks or adhesions in the neighborhood. These are the appendices which the X-ray now shows us retain the Bismuth hours or days after the rest of the meal has passed. They include the catarrhal, the lymphoid, and the minor kinks and twists — but their lumen is still free so that when their internal tension rises the discharge can escape into the cecum (and only cause a slight belly-ache or indigestion). (Fig. 4.)

The line to be drawn between No. 3 and No. 4 is merely defined by the obvious character of the kink.

5. Acute suppurative appendicitis of varying degrees.

A PERSONAL WORD TO THE READER.

There is no more need of your having your children's appendices removed than there is of your carrying life insurance or of your abstaining from liquor or of avoiding over work and over worry or of over speeding your automobile; but you will still probably do all of these things and will still submit yourself or members of your family to some eminent consultant for his opinion as to whether or not the occasional belly-ache is due to the appendix. The consultant may look wise but in a hundred cases he cannot show the wisdom of the doctrine of chances, unless there has been a previous definite attack of the symptom complex — general abdominal or epigastric pain, right iliac localization and *tenderness persisting at McBurney's point for a day or two after the pain has disappeared.*

If he wishes to make no positive mistakes he will add to this sequence, on the second day, slight fever and vomiting or nausea.

He cannot avoid negative mistakes for many cases with definite appendiceal lesions give no history of previous attacks.

Fig. 1.

This class includes kinks, bends, twists, short mesenteries, congenital adhesions and misplacements or other causes which render a partial obstruction of the lumen probable.   Such conditions predispose to retention of feces and bacteria and later prevent the exit of infected secretions.

They represent the next most dangerous condition to stenosis from post inflammatory stricture.

We all agree that No. 2 should be removed because it is really dangerous.

We all agree that No. 1 at times, and perhaps always, presents the same dangers in minor degree as No. 2.

Most surgeons seem satisfied and regard their operation as successful when they can demonstrate No. 3 to the patient or to the attending physician, but is it not more logical to remove No. 4 which has all the possibilities of the others? For it would save No. 3 the attack which caused his obliteration — it would save No. 2 the original attack which caused his stricture as well as the repeated later attacks — it would save No. 1 and No. 4 all the minor belly-aches which are relieved by the discharge of the contents of the appendix into the lumen of the intestine, and besides it would save the manifold dangers and complications of real acute suppurative appendicitis and its various sequelæ.

At least 50 per cent of mankind show No. 2 or No. 3; at least 25 per cent more show No. 1, and it is highly probable that of the remaining 25 per cent nearly everyone suffers from appendiceal belly-ache and reflex gastric indigestion at times. The X-ray is teaching us that these open "normal" appendices frequently retain food remnants hours and days after the rest of the meal has passed the cecum and yet the operation has no mortality and few complications as compared with acute appendicitis.

Strictured
or
Vicious appendix

Fig. 2.

In this class previous inflammation in the proximal portion has left cicatricial stenosis just as in stricture of the urethra. As long as there is active mucous membrane distal to the stricture there will be a tendency to recurrent inflammatory attacks.

This class includes cases of hard concretions and retained muco-pus or hydrops. If strictures were not present the concretions would be discharged. These are healing appendices for eventually repeated inflammation would destroy all the mucosa.

Strictures are most common at the points of kinking.

Obliterated
or   safe appendix

FIG. 3.

This class represents the healed or partially healed appendix. Obliteration is most common at the tip. The further the obliteration has progressed from the tip the greater the safety of the individual. Obliteration means that the mucosa has been destroyed by previous inflammation and that the discharge has escaped through the unobstructed lumen.

There is no good Indian but a dead Indian and there is no safe appendix but a completely obliterated one.

Normal
or
Belly-ache appendix

Fig. 4.

This class of normal appearing appendices covers a multitude of sins; the catarrhal, the injected, the lymphoid, the one with thickened muscular coats and all others which are not susceptible of pathologic proof. Presumably it may at times be as badly inflamed as the mucous membrane of the nose with influenza and yet by discharging through its lumen return to a normal condition without a trace of cicatrization. How many of the belly-aches of life it is responsible for we do not know, but they must be many for it is reasonable to suppose that most inflamed appendices discharge through their lumen, even when there is partial stoppage from kinks and twists.

Since the organ is abundantly supplied with lymphoid tissue, toxic conditions which affect lymphoid tissue in other parts of the body must affect it.

The X-Ray now shows us that the appendix often retains the Bismuth hours and days after ingestion.

The normal appendix has all the possibilities of evil great and small!

DISCUSSION OF ARTICLE XVII.

DR. P. P. JOHNSON, Beverly: This society is to be congratulated upon having such a paper presented with all the statistical points determined before the taking of the histories. Accurate statistics can only be arrived at in this way, and we can all appreciate of how little value they are when taken in the usual way from haphazard hospital records.

I am quite in accord with the statement that chronic appendicitis is much more common than we have supposed and I find that practically all of the appendices which are taken out in acute attacks show evidence of previous disease even if a previous history is lacking. It seems to me that we have but two cardinal symptoms, pain and tenderness, other symptoms being of no great value in making a diagnosis. Certainly I feel that these two symptoms should be present before operation can be advised.

Surgery does not seem to have progressed to that point where we can promise absence of complications. Therefore, I should hesitate to advise the removal of normal appendices. I regard constipation as being of no value as a symptom, but in my experience it seems to be present in fifty per cent of the cases.   To determine its relation to chronic appendicitis I have made X-Ray studies of these cases and in no case do I find stasis in the ileum or cecum except there be constricting bands or adhesions.

The question of *cæcum mobile* has also been intensely interesting to me, and for the last six months I have been making X-Ray studies before and in some cases after operations to determine whether there is any stasis. As a result of these observations I have come to the conclusion that stasis in the cecum is not a result of *cæcum mobile* alone; but is either a part of a general ptosis and atony or organic interference.   Therefore, fixation of the cecum seems an unnecessary operation.

In two recent cases I have found marked stasis in the cecum.   The first case showed a large mass in the cecum fifty-one hours after a Bismuth meal and persisting in spite of several enemata.   At operation the cecum was full of feces and tied down into the pelvis by adhesions resulting from

an old appendicitis. This was complicated by a Lane's kink and proximal to this four annular constrictions of the ileum. These constrictions were lined by small ulcers which proved to be tubercular.

The second case showed a large mass in the cecum at the end of twenty-four hours when the observations ceased. Operation showed also feces in the cecum, which was bound down into the pelvis by adhesions, and the first portion of the ascending colon rotated outward by Jackson's membrane as it passed to the parietal peritoneum, making a sharp angulation of the bowel.

I have not been so successful as Dr. Codman in relieving my patients of gas pains and discomfort following the operation by Crille's method of anoci association. Possibly my technique has not been so perfect. However, the principle seems to be so logical that I deem it worthy of further trial.

DR. J. B. BLAKE, Boston: Dr. Codman's paper was, as usual, original, careful, positive and thorough, even if we do not agree with him on every point. Under a misapprehension which was my fault, I had supposed that Dr. Codman was going to speak of the results of appendectomy and I had prepared my discussion along those lines.

I have been interested to find out whether the patients who had been operated could be considered well — in other words, to find whether the operation was a complete success. Although seventy-five patients were notified by telephone or card, less than one-fourth of them could be traced, illustrating the difficulty of tracing patients in a municipal hospital. The figures, therefore, are too small to be of convincing value, but what I did discover was sufficiently interesting and it seems to me sufficiently positive to be worth while.

The private cases were followed up after operation by my brother and myself. There was what might fairly be called a complete and satisfactory cure in four-fifths of them. At all events, the patients were free from the symptoms for which they had been operated, and they had nothing abnormal about the seat of operation.

Sixty per cent of the hospital cases, on the other hand, which had been discharged from the wards, had symptoms persisting which the operation might have been hoped to

relieve. These symptoms were either general or local, often local in the cases which had healed by first intention.

This emphasizes a point that every one knows but many forget — the importance of after treatment of appendicitis. It need not necessarily be confined to the surgeon, but may go perfectly, properly, into the hands of the family practitioner. It is very important; Patients should never be given a suggestion that the operation alone without after treatment is going to be effective toward complete cure, but should, on the contrary, be impressed with the great necessity of post-operative regulation.

The second point I wish to speak of is this: The medical community and the general public have been educated so well to the importance of pain in the right iliac fossa that we get cases early. Therefore, if we may occasionally open a case where the appendix seems normal we may not feel badly over it. On the other hand, the right upper quadrant has not received the same consideration from the general public. The right upper quadrant cases arrive at a much later period, as the community is not educated to the great necessity of early surgical interference in lesions of the region. When people have appendicitis they beg to get into the hospital and be operated, but with infections of the biliary tract, it is quite impossible to get them to substitute early surgery for long-continued medication.

DR. S. A. MAHONEY, Holyoke: I should like to inquire of Dr. Codman what methods he uses to carry out the anoci association in the technique, in a general hospital — whether he has a regular-trained set of nurses and attendants in order to carry out the treatment.

Also I should like to know what incision he makes in getting his appendix out. Whether he explores the entire abdominal cavity, in addition to the right iliac region, to see if there are any other lesions besides chronic appendicitis.

DR. CODMAN: The anoci association technique which I use is very nearly the same as Dr. Crile's except that I use novacaine, quinine-uria, and adrenalin together. They seem more efficacious than when used singly. He does not use adrenalin. The actual technique I have taken from observ-

ing him do it on three different visits to Cleveland. I am
sure that in my earlier cases I used it insufficiently, so that
the results were not quite so good. What I have done has
been merely to copy him.

In regard to the incision, I prefer a straight rectus incision
and I explore the whole right iliac region.   For instance,
there were twelve Lane kinks in the series of ninety-eight,
and I have forgotten just the number of Jackson's veils, but
those will be put on record with the paper.

ARTICLE XVIII.

THE VALUE OF THE ROENTGEN METHOD IN THE STUDY OF CHRONIC APPENDICITIS AND INFLAMMATORY CONDITIONS, BOTH CONGENITAL AND ACQUIRED, ABOUT THE CECUM AND TERMINAL ILEUM.

By Arial W. George, M. D.
AND
Isaac Gerber, M. D.,
of Boston.

Delivered June 10, 1913.

PLATE 1. CASE 1.—This plate shows a large intestine of the typical text-book type. (A) Appendix.
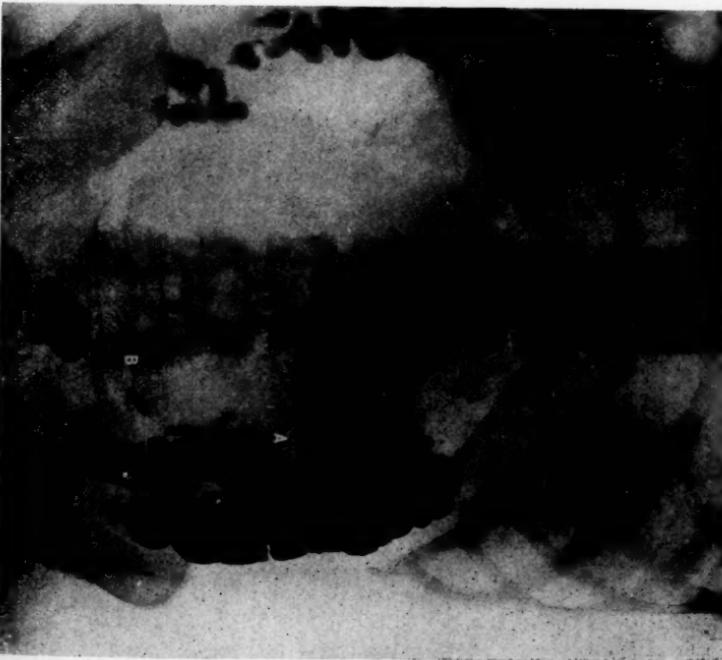
PLATE 2. CASE 2. — Plate made ten hours after the bismuth meal shows ileal stasis with a kinking of the distal portion of the ileum. (B) Appendix showing divisions which proved to be concretions. (A).
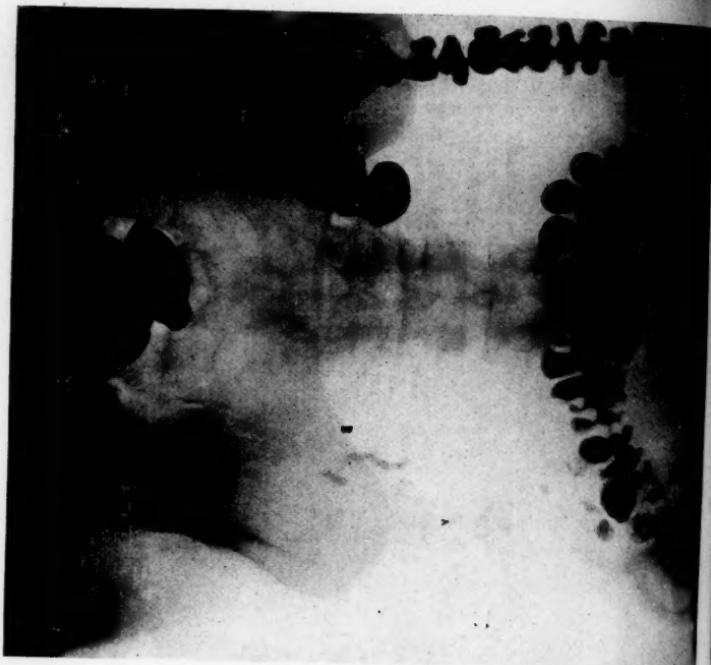
PLATE 3. CASE 2. — Plate made twenty-four hours later shows (A) cecum empty. (B) Appendix still retaining bismuth.
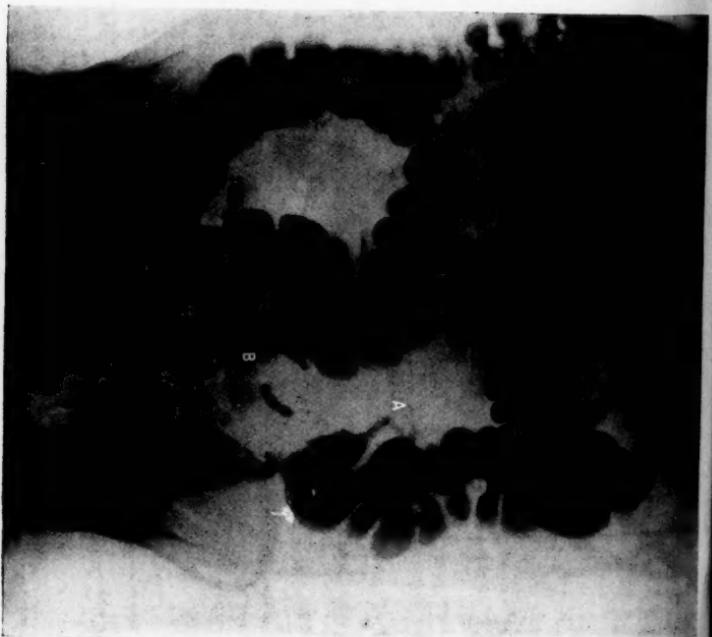
PLATE 4. CASE 2. — Plate made one week later. Bismuth enema, shows (A) patency of ileocecal valve allowing bismuth to pass back into the ileum. The same relative position of the ileum observed as in Plate No. 2. Appendix still full of bismuth from previous examination. Diagnosis: Chronic appendicitis with adhesions about the terminal ileum. Operation confirmed Roentgen diagnosis absolutely.

the cecum and proximal portion of the transverse colon (B), Appendix (A).

PLATE 5. CASE 3. — This plate shows a residue in the stomach. Marked ptosis of the transverse colon and ileal stasis (A).
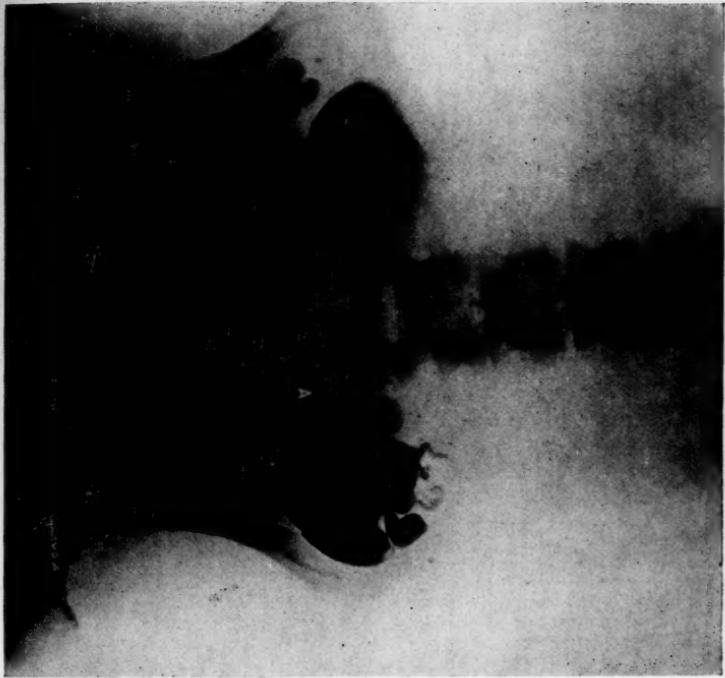


PLATE 6. CASE 3. — This plate shows the effect of adhesions about the cæcum and proximal portion of the transverse colon (B), Appendix (A).

PLATE 7. CASE 4. — Plate showing a fixed terminal ileum. (B) Stasis after twenty-four hours. The distal portion of the appendix (A) is obliterated by disease. Operation confirmed the Roentgen findings.
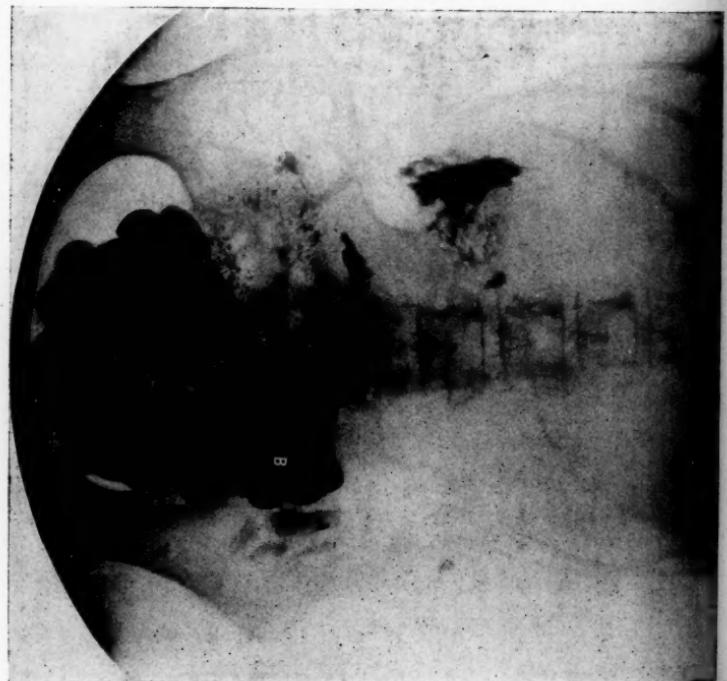
PLATE 8. CASE 5. — Marked ileal stasis after twelve hours due to Lane kink. Operation. (A) Cecum. (B) Ileum.

PLATE 9. Case 6. — There is marked fixity of the terminal ileum due to adhesion. Chronic appendicitis. Operation.

PLATE 10. Case 7. — Plate made twenty-four hours after bismuth meal. (A) Kinked appendix. (B) Ileal stasis. Diagnosis: Chronic appendicitis with adhesions. Operation confirmed Roentgen diagnosis.

PLATE 11. Case 8. — Roentgen diagnosis: Chronic appendicitis with obliteration of distal half. Operation.

PLATE 12. Case 9. — (B) Showing the effect of adhesions about the hepatic flexure. (A) Chronic appendicitis, kinked.
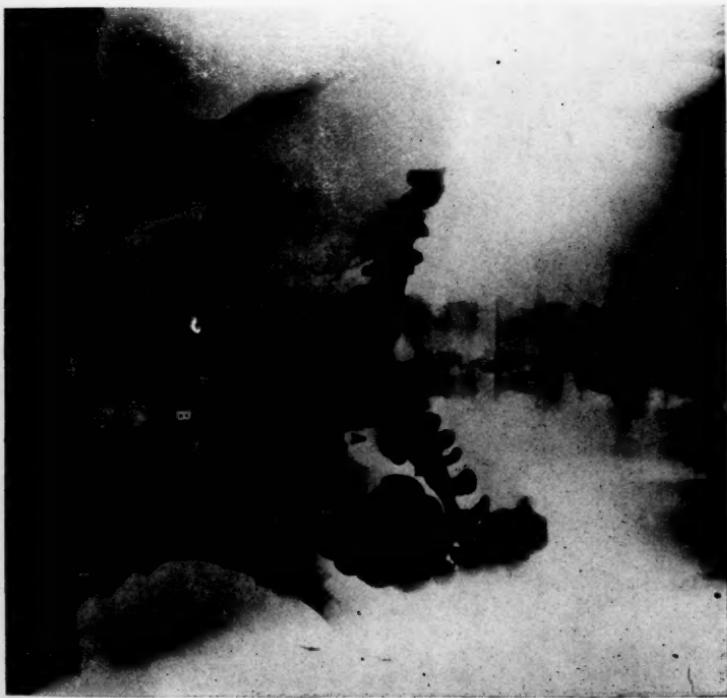
PLATE 13. Case 10. — Marked pericolitic veil and adhesions about the hepatic flexure. Operation confirmed Roentgen diagnosis.

PLATE 14. Case 11. — Cæcum mobile.

THE VALUE OF THE ROENTGEN METHOD IN THE STUDY OF CHRONIC APPENDICITIS AND INFLAMMATORY CONDITIONS, BOTH CONGENITAL AND ACQUIRED, ABOUT THE CECUM AND TERMINAL ILEUM.

We are presenting here a series of cases which illustrate just how we can make Roentgen diagnoses of surgical conditions in the right lower quadrant of the abdomen and neighboring organs. In practically all of these cases the clinical symptoms were very much alike. First and foremost was constipation, usually extending over a period of years; then there were more or less vaguely-localized abdominal pains, with frequent distention and flatulence. In some cases the symptoms pointed more towards the stomach — pain, pressure or distress after eating, heartburn, belching, nausea, frequent headaches. In one case there were vomiting attacks of increasing frequency, until practically nothing could be held on the stomach. Many of these cases had been treated medically for varying lengths of time, both by drugs and by dietetic regulation directed against either the stomach trouble or the chronic constipation. In none of these cases did the treatment give more than temporary relief; in some not even that. In most of them the true condition as shown by the Roentgen examination, and proved by later operation was not even suspected; although they were under the care of competent internists and surgeons. This was due not to any neglect on the physicians' part, but rather to the inaccessibility of this region to the ordinary methods of diagnosis. We shall not dwell here further on the clinical

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aspect of these cases, but merely describe their appearances
from the Roentgen point of view.

In our examinations we used our usual test meal, con-
sisting of 90 grams of bismuth subcarbonate in a mixture
of artificially-prepared buttermilk and water; in all about
500 cc. In some cases a bismuth enema was used to confirm
or clear up the information given by the meal. These cases
naturally divide themselves into five groups.

1. *Chronic Appendicitis.*

By this term we do not wish to indicate appendices
that have necessarily at any time undergone acute in-
flammation, but refer rather to those cases where the
appendix is either kinked or involved in adhesions. Of
course, many of these adhesions are of anomalous de-
velopmental origin, but their effect in producing symptoms,
and their Roentgen appearance, are the same as the
others. Chronic appendicitis may be shown in two ways:
First, by the ileal stasis which it produces; and *second,*
by actual demonstration of the kinked and adherent
appendix. By "ileal stasis" we mean retention of bis-
muth in the terminal loops of ileum for a longer period
than is normal. Normally, six hours after our test meal, the
bismuth should not only be out of the stomach, but also
nearly completely out of the coils of ileum. Many perfectly-
healthy persons, however, will show a small amount of bis-
muth still present in the terminal ileum at the six hour ex-
amination. To be safely classed as real ileal stasis bismuth
should be present at least twenty-four hours or longer. From
the presence of marked ileal stasis alone we cannot make a
diagnosis of chronic appendicitis; but we can sometimes
infer it. It is, however, just this method of inference that
has served to bring much of the Roentgen bismuth work
into disrepute among careful physicians. We feel that in

this, as in other departments of Roentgen diagnosis, the aim should be to find some factor that offers positive, not inferential evidence.

This positive evidence is found in the actual demonstration of the appendix itself, that is of the bismuth mixture within the lumen of the appendix. The fact that the appendix can be demonstrated Roentgenologically is today known to only a small proportion of our surgeons, and even of the Roentgenologists. Only two months ago, Groedel, one of the foremost of German Roentgenologists, published a paper in which he claimed to have demonstrated the appendix in three cases, all of which were pathological; and he showed a print of one. From this extensive series he concluded that the normal appendix cannot be demonstrated by the Roentgen ray; and conversely that an appendix which can be demonstrated by this method is pathological. Of course this evidence is ridiculously insufficient. Pathological appendices have been shown for many months by Jordan of London who does the Roentgen work for Lane at Guy's Hospital. In this country, Case of Battle Creek over six months ago published a large series of over sixty cases in which he had demonstrated the appendix, some normal, most of them pathological. Case also inclined to the view that an appendix that can be filled with bismuth, if not definitely pathological, is at least a potential danger. We will agree with him in those cases where bismuth remains in the appendix for forty-eight hours or more, when it has passed out of the surrounding intestinal tract. In the other cases, where the size, shape and position of the bismuth shadow correspond to a normal organ, we do not believe that the potentiality for danger is any greater than is always associated with any unremoved appendix. Since our attention was called to the appendix by Case we have succeeded in demonstrating this organ either normally or pathologically in about seven out of every ten cases examined. In many cases the

normal condition was verified at a later operation for other purposes.

A pathological appendix can of course only show itself, if its lumen is unobstructed, at least in part. It may show a bismuth mass which is sharply kinked in one or more places. There may be adhesions to itself, to the cecum, ileum, or even to the sigmoid. We have shown an appendix wrapped around and adherent to the terminal ileum so as to obstruct the latter. Retrocecal appendices can sometimes be shown distinctly. Often these are obscured by the dense mass of cecal bismuth; and will show up more clearly when some of the bismuth has passed out of the cecum. In many of the cases bismuth will persist in the lumen of the appendix for many hours after it is out of the cecum and ascending colon; in one of our cases as late as five days after the ingestion of the bismuth meal. Of course in these cases the appendix is definitely pathological, but usually the abnormal condition is manifested by accompanying adhesions or kinks. Occasionally an appendix which is not shown on the plate may be definitely filled out with the bismuth mass by massage under fluoroscopic control.

2. *Lane's Kink.*

This is the condition, so much emphasized by Lane, where the terminal loop of ileum is fixed by one or more bands, either congenital, developmental or inflammatory. This condition as shown by the Roentgen method has, first of all, marked ileal stasis. This alone, however, is of little value. The actual demonstration of the distended and fixed terminal ileum is the real diagnostic point. This loop of intestine will be found in an abnormal and definitely-fixed position, at different times during the examination, and even on different days. The fluoroscopic examination here is very important. With the fluorescent screen we can manipulate and show that the terminal loop of ileum is really fixed.

3. *Jackson's Membrane.*

This condition is sometimes called "membranous peri-
colitis," and is another condition where opinions are divided
as to whether the cause is inflammation or anomalous de-
velopment. We are not concerned here with the etiology,
only with the demonstration of the condition by the Roentgen
method. The presence of the membrane, which runs across
the ascending colon and on to the proximal transverse colon,
is shown in several ways: First, there will be more or less
ileal stasis. This, however, is frequently due to the accom-
panying Lane's kink or chronic appendicitis. Obstruction
in the ascending colon is usually present, and is shown by
retention of bismuth in this part and in the cecum for twenty-
four hours or longer. A bismuth enema will also sometimes
show obstruction at the same place with perhaps acute an-
gulation of the proximal transverse colon. However, the
demonstration of ileal stasis and colonic obstruction is not
enough. We must demonstrate the actual effects of the ad-
hesions themselves upon the adjacent parts. Single plates
which show apparent "matting together of cecum, ascending
colon, and hepatic flexure" are not conclusive. The diagnosis
of Jackson's membrane from this evidence alone is likewise
shrewd guesswork. Real positive evidence can only be ob-
tained by manipulation under the fluoroscope where the
effect of the adhesions can readily be shown, or by demon-
stration on plates of the peculiar filling mechanism which we
have found to be associated constantly with Jackson's mem-
brane.

When the cecum is only partly filled with fecal material
the ascending colon and transverse colon may be some dis-
tance apart and apparently not connected. However, as the
cecum and ascending colon become filled more and more
with ileal contents, these adhesions begin to show their pres-
ence by pulling the proximal transverse colon towards the

ascending colon. Finally we have the characteristic "double-barrelled shotgun" effect of the two adjacent colonic parts. At this time under the fluorescent screen these cannot be separated by manipulation. This pulling together of the ascending and transverse colons as the result of filling is characteristic for these pericolitic adhesions only. With an atonic cecum (Typhlatony) we may have ileal stasis, and likewise a dilated cecum with abnormal bismuth retention. Here, however, we do not have the above-mentioned filling mechanism; and we cannot demonstrate adhesions under the fluoroscope. With this condition we have the so-called "ascendens" type of chronic constipation which is a subject for medical, not for surgical treatment.

4. *Adhesions.*

This group of cases we will pass over rather rapidly. We have found many cases of chronic constipation where the cause, as shown by the Roentgen ray, was adhesions of the sigmoid to the cecum from old pelvic inflammation; or the transverse colon may have been adherent to the ascending colon or cecum as the result of duodenal ulcer, gall bladder disease or old appendicitis. In these cases the demonstration of obstruction and ileal stasis was likewise not as valuable as the fluoroscopic demonstration of the adhesions or of their peculiar filling mechanism. In these cases the bismuth enema has been valuable because by its use we have been able to bring the colon more nearly to its normal position under complete filling. Acute angulations due to adhesions show very definitely by means of the enema.

5. *Cæcum Mobile.*

This is a condition which, although not found in this particular series of cases, deserves mention here, because of the emphasis which has been placed upon it of late by surgeons like Wilms and others. This anomaly of colonic fixation can

readily be demonstrated by the Roentgen method. The cecum and ascending colon are found not only to be in an abnormal position, perhaps in the median line, or to the left; but under the fluoroscope they can be very readily moved about. Incidentally, the diagnosis of left-sided appendix can be definitely confirmed.

Summary.

In a series of cases which clinically show severe constipation, and more or less indefinite gastric symptoms, examination by the Roentgen ray has shown the causes to be definite surgical conditions in the right lower quadrant. In all of these cases the demonstration of mere ileal stasis or obstruction is not as important as the more positive demonstration of the actual conditions.

In chronic appendicitis the kinked and adherent appendix is shown.

In case of Lane's kink we can demonstrate the fixed and distended terminal loop of ileum.

In cases of Jackson's membrane we can show the effect of the adhesions under the fluoroscope, as well as the presence of a characteristic mechanism of filling.

Various adhesions in this region as the result of old inflammatory disease or congenital anomaly can also be shown in the same manner.

Cæcum mobile and left-sided appendicitis can be readily demonstrated.

ARTICLE XIX.

CERTAIN OBSERVATIONS UPON TWO HUNDRED CASES OF GASTRIC DISEASE.

BY CHARLES L. SCUDDER, M.D.,
OF BOSTON.

DELIVERED JUNE 10, 1913.

CERTAIN OBSERVATIONS UPON TWO HUNDRED CASES OF GASTRIC DISEASE.

We surgeons believe that today most cases of chronic gastric and duodenal ulcer, and all cases of stomach cancer, are best treated by surgical measures. At some future time I intend reporting in detail the histories, the surgical treatment, and the results of the 200 cases of disease of the stomach that have been under my care. At this meeting I wish to direct attention to certain things which have interested me in the study and care of these cases of gastroduodenal symptomatology. I hope that these observations may prove interesting, and perhaps helpful, to those concerned with the varied problems of gastric surgery.

The majority of these cases have been studied in the Medical Service at the Massachusetts General Hospital. One hundred and thirty-eight cases, or over eighty per cent, I have operated upon. There were forty-nine cases of malignant disease. There were seventy-two cases of chronic ulcer. There were seventeen cases of congenital stenosis of the pylorus; three of these cases of infantile stenosis were almost starved to death when operated upon — they died following the operation. The other fourteen cases are living and well.

There were two deaths among seven perforated ulcer cases. Of the sixty-five nonperforating ulcers three died. There was one death among the forty-nine cancer cases.

In the last one hundred and three operations there was one death. There were no cases of postoperative pneumonia. The anesthetic in each case was ether, administered

by the drop method, at the hands of a skilled nurse
anesthetist. Occasionally gas was administered before
giving the patient ether. There were no cases of vicious
circle. There have been no jejunal or gastro-jejunal ulcers
following operation in this series. The evidences of shock
following these operations have been absent. There has been
no case of postoperative hemorrhage. The course of the
case immediately following operation has been uniformly
smooth. My assistants, and I, have been impressed by
the quiet, uneventful convalescence in these cases. I do
not believe that Crile's anoci association method is appli-
cable as a routine. There are selected cases, undoubtedly, in
which it is applicable.

The above experience leads me to regard the ordinary
plastics upon the stomach, duodenum and upper bowel, when
done under controlled conditions, as comparatively safe
operations.

The mortality following the operations in this series is
comparatively low. This low mortality is due to several
facts. The operation was done aseptically, bloodlessly, with
little trauma in handling and sponging, with no exposure of
adjacent parts, with mechanically-perfect suturing, without
tension upon the parts involved, with anatomical nicety,
with carefully-conducted anesthesia, with painstaking care
for details, and with celerity. Plastic operations upon the
stomach done under the above conditions are bound to be
followed by a low mortality, barring surgical calamities like
pulmonary embolism, unexplainable infection, the slipping
of a ligature, or a pneumonia.

The low mortality which surgeons are able to attain in
this group of diseases develops the confidence of the medical
practitioner in surgical measures. The medical practitioner
is likely to entrust the proper cases of stomach and duodenal
disease to surgery because of the low mortality.

The increasing absence of the disagreeable and dangerous

sequelae of operation likewise tends to inspire the physician with trust in surgical measures in suitable cases.

The lower mortality and the diminishing postoperative sequelae are two notable and comparatively recent achievements of gastric surgery, certainly, in this community.

Syphilis.

I am impressed in reviewing these cases by the part which syphilis plays in the etiology of chronic stomach disease. In several cases a positive Wassermann reaction and a history of syphilitic infection have made it seem almost certain that the stomach lesion was luetic.

Syphilis of the stomach is more common than generally has been supposed. It is a tertiary manifestation. A multiplicity of lesions are possible. These lesions may be a gumma tumor, or ulcerations in the stomach wall involving the mucosa, or adhesions extending from the stomach to neighboring organs. Syphilis of the central nervous system with symptoms of gastric crises may confuse the picture, when only the spinal fluid will show evidences of the infection. The symptoms of syphilis of the stomach may resemble chronic ulcer — or even cancer — differing from ordinary ulcer in their lack of regularity and persistence. In all of my suspected syphilitic cases there have been many peritoneal adhesions.

I believe that the Wassermann reaction should be tried upon every case of gastric disturbance with chronic ulcer symptoms. If there are no mechanically-obstructive symptoms and the Wassermann test is positive, then antisyphilitic treatment should be used. Failure of the treatment should be followed by surgical measures. Of course, in the case of obstruction, even if syphilis is present, ordinary surgical measures should be employed at once.

The surgeon should arrive at a diagnosis independently of the medical practitioner, who, naturally, first sees the

gastric patients. The patients who eventually find their way to the surgeon for treatment of chronic dyspepsia form only about from ten to fifteen per cent of those suffering from dyspeptic symptoms.

The patients in my series sought medical advice for various reasons: — Because of vomiting, because of hemorrhage, because of pain and distress following food, because of increasing weakness, and because of inability to work at the usual occupation, and all of them came because medicine failed to cure.

The cases of dyspepsia which the surgeon sees have proved rebellious to drugs and diet. Hence the surgeon is apt to have a low opinion of medical treatment. There are, no doubt, cases of ulcer which heal under medical care. I believe, however, that there are many cases of chronic ulcer whose symptoms are ameliorated by medical treatment, but which do not heal. These are the cases who, after years of invalidism and recurring attacks, may be and are cured by operation. The average duration of symptoms in my series of cases in the chronic ulcer group was seven years; in the cancer group three and one-half years. Many individual cases were of much longer duration.

I have made mistakes in diagnosis in the following cases:

Diagnosis of gastric ulcer in twelve cases proved to be adhesions in one case, no pathology in three cases, syphilis, but not of the stomach, in one case, leioma in one case, and appendicitis in six cases.

A diagnosis of duodenal ulcer in three cases proved to be Lane's kink and appendicitis in one case, sarcoma of the stomach in another, and appendicitis in the third.

A diagnosis of carcinoma of the stomach in two cases proved to be gastric ulcer in one case and duodenal ulcer in the other case.

In one doubtful case a diagnosis of stomach, gall bladder or appendix disturbance proved to have no visible pathology.

There were, therefore, nineteen diagnoses which were not established.   And there were included in these mistaken diagnoses four cases which were found to have no pathology. In any case in which no pathology was found, it is, of course, possible that a lesion existed and that it will become more apparent later, in a renewal of symptoms, or it may be discovered at some future operation.   The study of these cases without apparent pathology will be, therefore, worth while.

Diagnosis.   I have been most assisted to a diagnosis of chronic ulcer by a carefully-elicited story of the onset and course of the symptoms.   Definite pain in the stomach region has been the most constant symptom.   The hunger pain, so-called by Moynihan, has been found to be associated so frequently with ulcer on the gastric side of the pylorus that I am inclined to think that it is not diagnostic of duodenal ulcer.   As a matter of fact there is little practical use in the preoperative differential diagnosis between chronic duodenal and chronic gastric ulcer.

One examination should not suffice for the HCl test, for the blood test or for the stasis test.   The real value of these examinations can be determined only by repeated tests, especially in cases of doubtful diagnosis.

In the absence of other causes for hemorrhage, blood in the gastric contents and in the stool suggest ulcer or cancer. A very severe hemorrhage is oftenest associated with ulcer. A dribbling of blood in the bowel, occult blood in the stool, suggests ulcer or cancer.   The finding of blood in the stomach contents or in the stool is not essential to the diagnosis of ulcer.   Hypersecretion suggests ulcer.

I find in my series several cases in which even with definite gastric symptoms and hemorrhage, hemorrhage being perhaps the chief sign — that at operation no pathology was discovered.

In a man past middle life a sudden onset of persistent gastric symptoms suggests cancer.   The earlier ulcer symptoms,

which are so often found antedating the cancer symptoms, may have been forgotten and so thought not to have existed.

X-ray. There is no doubt in my mind that the value of x-rays following a bismuth meal in suspected cases of chronic ulcer and cancer, is very great indeed. I am positive, moreover, that constancy in the variation from normal as determined by repeated x-rays is essential to a diagnosis. The single x-ray plate has little value. Fluroscopic examination combined with the plate method gives the maximum evidence. Departures from the normal motility of the stomach, irregularity in the outline of the stomach wall, variations from the normal position of the stomach, evidences of pathology outside or inside of the duodenum — all may be determined today with such accuracy by the skilled Roentgenologist that I believe every case of suspected gastric and duodenal lesion should have complete x-ray examination.

I have taken the following attitude toward chronic ulcer cases before operation: All cases showing stasis should be operated upon at once. A posterior, no-loop gastroenterostomy is the preferable operation. Every case which has had a month to six weeks of the best medical treatment in bed and has relapsed and remained uncured should be operated upon.

I believe that plastics should be done on the stomach only in the presence of definite demonstrable pathology. At operation only those chronic ulcers should be excised which can be readily removed. If excision is undertaken it should be through the entire transverse diameter of the stomach. This will give a better functional result than when the ulcer is simply excised from the stomach wall. If an ulcer is simply cut from the stomach and the stomach deformed by suture then a posterior gastroenterostomy should be done. The motility of the stomach is sufficiently impaired in some cases to make this a good general rule. An ulcer on the anterior

wall of the duodenum may be excised, but it is hardly nec-
essary.

If the ulcer is duodenal a thorough folding in of the peri-
toneum and duodenal wall should be done, followed by a
posterior gastroenterostomy. This has been wrongly called
"infolding of the ulcer." The ulcer is really everted into
the bowel.

Ulcers away from the pylorus, if not resected, will prob-
ably heal more quickly if a posterior gastroenterostomy is
done. Bile and pancreatic juice gain access to the stomach
and bathe the ulcer in an alkaline medium which facilitates
healing.

I am not yet convinced that the likelihood of cancer de-
veloping upon ulcer is so great that I would resect every
accessible ulcer from the stomach. Very many ulcers will
never become cancerous, for all ulcers are evidently not
potentially malignant.

Kocher has reexamined eighty patients demonstrated at
operation to have had chronic ulcer (1890–1912), and none
of these cases in 1912 has developed carcinoma. Seventy
of these cases had had gastroenterostomy done and ten were
resected.

I believe resection may be preferable, in certain selected
cases, if it can be done easily and with little additional risk.
The mortality rises, however, in a large series from one or
two per cent for posterior gastroenterostomy to eight to ten
per cent for partial gastrectomy. This difference in per-
centage is to be reckoned with without a doubt. ·

It is impossible at times for the surgeon to tell at operation
whether the tumor is that of cancer or ulcer alone. If the
tumor is at the pylorus and extends both into the stomach
and into the duodenum, it is probably ulcer, for cancer of
the pylorus is most unusual. When the surgeon is in some
doubt and the tumor is removable it should be removed. I
have noticed in cases of ulcer that there is a red dimpling

over the surface of the peritoneum covering the ulcer —
minute red spots appear to gentle sponging with gauze.
Whether this is constant for ulcer I am not prepared to say.
It is suggestive.

Cancer.

Cancer of the stomach when seen by the surgeon is either
curable or it is incurable. The curable cases are rarely
seen. They should be operated extensively and thoroughly.
It is hoped by the advocates of the frequent removal of chronic
ulcer that thereby the cure of incipient cancer may be in-
creased. In only about eight per cent of my series was it
feasible to attempt partial gastrectomy. I have been very
much impressed by the few cases in this series of gastric can-
cer suited to radical operation. It is well to study the signs
of inoperability. Resection of cancer of the stomach should
not be done if there is great weakness of the patient, if there
are evident metastases, if there is free fluid in the abdominal
cavity, if there are cancerous adhesions to neighboring parts,
and if the disease cannot be readily reached, that is, if the
disease is inaccessible.

The size of the cancer tumor may bear no relation to the
curability of the disease.

Gastroenterostomy is a poor palliative measure in cancer
of the stomach. The length of life secured is but about four
months. It is better, if practicable, to resect as a palliative
measure, and rid the patient of a sloughing mass of cancer,
not being content simply with a posterior or anterior gastro-
enterostomy. The length of life is longer after palliative resec-
tion than after palliative gastroenterostomy, even more
than double as long.

The end results of the surgical treatment of chronic ulcer
in my series, so far as they have been obtained, are most en-
couraging. Pyloric obstructive cases are cured in the ma-
jority of cases. Duodenal ulcer cases are almost all cured.

Ulcer in the body of the stomach away from the pylorus are benefited and many cases are cured.

It is an interesting fact that the cases of gastric symptomatology which at operation had no gastric pathology, but had an appendectomy done are very generally well.

I believe that these obstinate chronic ulcer cases which have resisted medical treatment, should, after operation, continue to have medical treatment and a regulated diet. I believe that such cases should be led to expect necessary treatment for at least one year after the operation. The operation should be looked upon as only one therapeutic measure instituted by the surgeon in conjunction with medical therapeutics for a disease the etiology of which is still unknown. The results of surgery in the group of chronic ulcers has certainly been very satisfactory.

The details of the results following surgical treatment in my series of cases I hope to have the pleasure of reporting at some future time.

The diminishing surgical mortality, the few painful operative sequelae, the encouraging results from surgical treatment — all make me optimistic that the physician will entrust more and more of the difficult gastric cases to the care of the surgeon.

DISCUSSION OF ARTICLE XIX.

Dr. F. B. Lund, Boston: We are to be congratulated upon having such a thorough and entirely adequate presentation of the position in surgery of ulcer of the stomach as Dr. Scudder has given us. He has certainly left very little for anybody to say in discussion in the way of disagreeing with either the character of his work or with his conclusions. This subject in surgery is one which has interested me for a great many years, and in which I have done a considerable amount of work.

The medical cure of chronic ulcer of the stomach, I think we can all agree is a rarity. These ulcers may heal, but the

condition is not altered by the healing of the ulcer. By en-
larging the pylorus or by a gastroenterostomy, certain con-
ditions, either mechanical or chemical, are altered so that
the ulcer not only heals but remains healed. The first rough
surgery that we did fifteen or twenty years ago was for per-
forations of the stomach. On account of improved technique,
our results in perforation are better now.

The second kind of cases that almost invariably did well
when operated upon were strictures of the pylorus. Then
duodenal ulcers almost always healed; then it was found that
chronic ulcers of the stomach which were at some distance
from the pylorus did not heal so well. The adoption of the
no-loop gastroenterostomy improved enormously our results
by doing away with the vicious circle.

Now a point of the greatest importance, to which Dr.
Scudder alluded, is the difficulty of making the differentiation
between chronic ulcer and cancer of the stomach, and deter-
mining in a given case what action the surgeon shall take.

Gastroenterostomy has a mortality of perhaps from 2 to 5
per cent; excision for cancer where you must go wide beyond
the margin of the stomach, from 8 to 10 per cent. The indu-
ration which attends a chronic ulcer may be indistinguishable
from that of a cancer. Cancer almost never starts in ulcer
of the duodenum, and here we are almost always safe in
depending upon infolding of the ulcer and gastroenterostomy.
The condition is different where we are dealing with saddle
ulcers on the lesser curvature at a distance from the pylorus.
They sometimes are very slow to heal, or do not heal at all,
after a gastroenterostomy. We have here to consider the
ability of our patient to stand an operation of greater length.
We ought not to undertake the excision unless the patient
is in good condition to stand it; and, also, these ulcers some-
times do heal after a simple gastroenterostomy. Excision
for chronic ulcer of the stomach if very small need not be
as extensive as excisions for cancer. If you are excising the
stomach for a large saddle ulcer, then it is wise to take out
a complete sleeve of the stomach as you would in a partial
gastrectomy for cancer. If you have simply excised this
great ulcer, what have you left behind? You have left the
stomach as it was before, except for increased deformity,
and you have a long line of freshly sutured wound which

may produce another ulcer. A gastroenterostomy should be done to prevent any trouble which may come from the deformity and to decrease the liability of recurrence.

Adhesions which sometimes deform the stomach follow after gastroenterostomy. The ends of the pylorus remaining open, the food has two avenues of exit: part goes each way, and indigestion results. This is reduced by measures which close the pylorus. Infolding of ulcers at the pylorus is efficient, and it is not necessary to excise these ulcers. If infolding has not been successful and the patient suffers from the opening remaining patent, the only way to put a stop to his symptoms is to do a second operation and to divide entirely the pylorus, turning in the duodenal and pyloric ends.

DR. D. F. JONES, Boston: In regard to stomach diseases, I want to say that I agree entirely with what Dr. Scudder has said in his paper.

Then to supplement his paper in a way, it may be of interest to you to report a few cases that have been done for a number of years; cases of gastroenterostomy for duodenal ulcer. I have had time to get reports back from twenty-nine cases, all having been done from two years to nine years. Of these cases, there were two which died. One case was due to persistent vomiting, and the other was an empyema which refused to be operated upon. He was an old man of sixty-eight years, and had an infection of the pleura or lung probably from embolus. He went home at the end of five weeks, refusing operation, and died. The case of persistent vomiting, I think, would not have died at the present time. There are twenty-seven cases living and well. Of these the reports are that they are all very much improved. I cannot say with Moynihan, that they are absolutely well, because very few admit that they are absolutely relieved of their symptoms, and I think that if any of us will look over his cases and get a personal examination, he will find that very few patients will admit that they are absolutely well. One of the worst cases, a professor at Harvard, and therefore an intelligent man, thought he was not very much improved. I had a letter from him only two days ago, in which he said that while he was not entirely well, he would willingly go through the operation again, for the relief that he had gotten

from it. The others were very much improved, and have
written very grateful letters, and many of them came in to
see me to let me know how well they were. In spite of that,
if you question them, you will find that they are very glad
to cover up little defects and tell you they are well, while
as a matter of fact they do have a few symptoms referable
to the stomach.   All of my cases have gained weight, and
are very much improved in every way.

Now as to the technique, Dr. Scudder says that by carrying
out the technique very carefully, he thinks that everyone
can get good results. It is very simple — the mere suturing
of the jejunum to the stomach — but it seems to me there
is more than that. It is the ability to place the jejunum in
such a way that it will not kink, either at the inlet or the
outlet. I have seen the jejunum placed in every possible
way, vertically, transversely, obliquely, the current in the
jejunum with and against that in the stomach, and even
with the outlet at the highest point of the stomach opening,
with the outlet exactly on the greater curvature, and an inch
and a half above it; they have all done well because they did
not happen to kink at either the inlet or the outlet. I am
convinced that the calamity of vicious circle is due to a kink
at the inlet or outlet, and not to the length of the jejunal
loop, or the method of placing the jejunum on the stomach.
This kink at the outlet is due I believe not infrequently, to
a short mesentery of the jejunum, which tends to pull upon
the jejunum at the outlet, and thus shut off the outlet.

In regard to gastric ulcer, I am convinced that excision
of the ulcer alone, is an operation of very little value. A
rather difficult operation has been performed to get rid of an
ulcer and the resultant scar, but a longer scar is left and
nothing is done to get rid of the cause of the ulcer.

If anybody can tell me how you improve the patient's
condition by taking out an ulcer of that size, then I will
admit that it is good.   If you are going to excise the ulcer,
I believe that gastroenterostomy is necessary.   To prove
that gastric ulcers do get well under various treatments —
I have heard from the following patients: one excision of
the ulcer alone had a perfect result; one excision of the
ulcer with no relief whatever; one infolding of ulcer, patient
relieved for over two years; two cases of gastroenterostomy

for saddle ulcer, with perfect relief.   In one case the ulcer was so extensive that I could not do a posterior gastroenterostomy, so I closed the abdomen.   That was four years ago, and the only condition left is the morphine habit, the patient being absolutely relieved of her symptoms.

DR. E. A. CODMAN, Boston: There are a few things I should like to say about Dr. Scudder's cases.   It has fallen to me to follow Dr. Scudder in doing the stomach cases at the hospital, and although the numbers of my cases are very much fewer than Dr. Scudder's, my mortality is already higher.   Now, I have seen Dr. Mayo and Dr. Moynihan do a good many cases each, of gastroenterostomy, and I have never seen the operation more skilfully done than by Dr. Scudder.

There is one serious criticism, however.   He tells us that he had one death in cancer of the stomach.   Now I feel that an operator as skilful as he is should have a larger death rate and should have attempted to do gastrectomy on a larger proportion of these stomach cases, for as he says, there is very little relief from gastroenterostomy in cancer of the stomach.

Somebody must forge the way in doing gastrectomy. Even if there is a metastasis in the liver or other parts of the body, it gives a much longer period of relief than gastroenterostomy.   I have seen relief for four years where there were obvious cancerous glands left, and I am sure that in a series of this kind the mortality should be at least as high as ten per cent, because more and more desperate cases should be attempted.

I think it is only fair to the patient to try the faintest possibility of removing the disease.

DR. T. W. HARMER, Boston: The detection of stasis is important.   Failure of the unaided stomach tube (regardless of the posture of the patient) to reveal stasis, which is demonstrable by the bismuth meal and Roentgen ray is a not infrequent experience.   This has led Dr. Walter J. Dodd and myself to observe by the fluoroscope the courses taken by stomach tubes in a number of cases.   In some, the tip of the tube reached the most dependent portion of the stomach.

In others, the tip curved to one side immediately upon leaving esophagus and became impinged against the stomach wall. With the passage of more tube, with the tip so fixed, a dependent loop of the tube developed in the lower portion of the stomach until finally the tip slipped upward. Stomach tubes are commonly kept coiled. The tube acquires a tendency to curve and we believe it is the tendency so acquired which is responsible for its deviation from a straight course after emerging from the lower end of the esophagus. If the curve of the tube accommodates itself to the curves of the stomach wall and, if the tip does not become impinged against the stomach wall, the tip will reach the most dependent portion of the stomach. Deductions will be correct. If, however, the curve of the tube does not accommodate itself to the curves of the stomach wall and the tip becomes impinged against the stomach wall, the tip may not reach the most dependent portion of the stomach. Deductions will be incorrect. The tip may only skim the surface of the residuum. The degree of stasis will be underestimated but analysis of the contents may reveal stasis. In some cases, however, even considerable amounts of residuum may entirely escape detection by the unaided tube. In cases of ptosis the degree of displacement may be underestimated and an insufficient amount of tube passed. Failure to recover gastric residuum with an unaided stomach tube from a fasting stomach or after the ingestion of a test meal cannot be accepted as conclusive evidence of the absence of gastric stasis.

DR. MURPHY, St. Louis: I hesitate to bring in a note of discord as regards the efficiency of gastroenterostomy with a patent pylorus. Now the cases that I have seen, unless there was a mechanical obstruction of the pylorus, have not done well permanently with gastroenterostomy. We have come to believe that in these cases with nonobstructing ulcers, we ought to do a resection of the ulcer-bearing area of the stomach, and a gastroenterostomy and that with nonobstructing ulcers of the duodenum, a complete section across the pyloric end of the stomach, together with gastroenterostomy.

Among other points that Dr. Scudder made, there is one that, it seems to me, more and more the men who are doing

gastric surgery will agree with most heartily; that is, there is a very low mortality in these cases. I would also agree with his opinion that syphilis is not infrequently associated with these stomach lesions.

There is another point that interested me, and that is the possibility of overlooking these small ulcers. I have had two experiences recently in which, without the positive statement of the x-ray men that the ulcers were there, I should have overlooked small ulcers, one in the fold of the pylorus, and the other on the lesser curvature at some distance from the pylorus.

In cases without pyloric obstruction that do well with gastroenterostomy, I should feel that they belonged to the class mentioned by Dr. Jones, which do well in spite of everything.

DR. SCUDDER: There is just one matter that I want to speak of and that is the employment of jejunostomy in a certain group of cases. It seems to me that jejunostomy has come to stay. It is a surgical procedure of considerable value in a selected group of cases. Whenever an individual is unable to stand any prolonged operative procedure upon the stomach on account of great loss of blood and because of great weakness jejunostomy may be very helpful. I have in mind one case which will illustrate what I mean. A man came to the hospital in a weak, emaciated condition, and was bleeding from the bowel. It was thought that he had duodenal ulcer. A few days' rest in bed resulted in a little improvement in his condition. Subsequently, however, he ceased to improve. Operation was done and a jejunostomy performed. There was found to be a tumor in the stomach wall. It was evidently impossible to remove this tumor by partial gastrectomy as the man's condition would not warrant it. The jejunostomy enabled the man to take nourishment, the symptom of vomiting disappeared, he gained in flesh and in strength, and at a subsequent time the tumor was removed successfully. Such a case as this illustrates the value of jejunostomy. I believe that this procedure has also a very definite place in the treatment of chronic ulcer in the case of individuals very much run down, jejunostomy being used as a preliminary step in the surgical procedure for ulcer.

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